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POTASSIUM DEFICIENCY IN ENTERO-COLITIS IN INFANCY: ITS CLINICAL FEATURES, TREATMENT AND PREVENTION.[1]

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THE object of this paper is to record the clinical features and the treatment of 13 patients with entero-colitis who developed potassium deficiency during their illness, to indicate how a diagnosis can be made and to suggest measures for the prevention of this complication. American pædiatricians, especially Darrow (1946, 1949), Gamble (1950) and Rapoport (1947), have largely contributed to our knowledge of the disordered physiology of water and electrolyte in infants with diarrhœa. Experimentally Darrow (1946) and others have demonstrated that there is a steady though very variable loss of potassium in the stools, and if the diarrhœa persists serious depletion of cell potassium occurs unless potassium is given to replace this continued loss. Balance experiments have shown potassium depletion in all patients with moderate diarrhœa. In addition, it has been shown that cell potassium is usually partly replaced by sodium, and that if sodium is given in large quantities it still further replaces cell potassium. Considerable reduction in the mortality of patients with entero-colitis has been claimed by Govan and Darrow (1946) and others following the routine administration of potassium, either orally or intravenously, to all patients.

[1] Read at a meeting of the Melbourne Pædiatric Society, August 8, 1951.

Clinical Material.

Thirteen patients with severe potassium deficiency were observed in a series of 496 infants admitted to the Children's Hospital, Melbourne, with entero-colitis from January, 1950, to July, 1951. The majority of these 496 infants were severely ill, as they were patients requiring special nursing treatment, and frequently intravenous therapy. The larger number had a non-specific infection, the remainder specific infections with either one of the Salmonella organisms, *Shigella Flexner* or *Shigella sonnei*.

An appreciation of the broad outline of treatment of these infants with entero-colitis is necessary in order to indicate those patients likely to develop severe potassium deficiency. All infants were given a preliminary period of starvation of milk for eighteen to forty-eight hours, depending on the severity of the illness. During this time water, sodium chloride and glucose were given by mouth in amounts that the infant could tolerate. Skilled nursing would often obviate the necessity to give fluid intravenously. Infants with circulatory failure from dehydration and toxæmia were disturbed as little as possible and were given oxygen and an intravenous infusion of normal sodium chloride solution in 5% glucose in water (up to 30 millilitres per kilogram) and, if toxæmia was severe, a transfusion of blood or serum. After improvement N/4 sodium chloride solution in 5% glucose in water was infused, and a similar fluid was given orally for twenty-four to forty-eight hours. If the infant was not severely dehydrated or shocked, warmth and frequent small amounts of N/4 sodium chloride solution in 5% glucose in water were given orally for a similar period. The quantities of water, sodium chloride and glucose administered were estimated from a knowledge of the infant's normal daily

requirements together with an arbitrary estimation of the losses that occurred from diarrhœa and vomiting. No additional potassium was given to any of these babies. After a period of eighteen to forty-eight hours' starvation dilute milk feedings, either of skimmed milk or milk of low fat content, were commenced and the amount and strength gradually increased as the infant improved. With good nursing and this *régime* of fluid administration and feeding most babies made satisfactory progress. The mortality rate over these 496 patients was just under 6%.

However, there was a group in which the diarrhœa was severe and persistent, oral feeding was difficult owing to vomiting or poor sucking, and intravenous therapy for long periods became necessary to supply sufficient water and electrolytes. In this group 13 patients developed severe potassium deficiency with alarming clinical symptoms; in nine cases it seemed to be the sole factor causing symptoms, and in four there was an associated infection—bronchopneumonia in three and pyelonephritis in one. A study of the nine patients concerned has given, I believe, a reasonably reliable clinical pattern of potassium deficiency in infants, as it seemed to be the sole factor causing symptoms. The method of study has been that of close observation and recording of clinical data, and the estimation of body weight and the electrolyte pattern in the serum at suitable intervals. Sodium estimations were made by the gravimetric method of Butler and Tuthill, potassium by the method of Kramer and Tisdall, chloride by Whitehorn's method, alkali reserve by the Van Slyke volumetric method, and protein by the copper sulphate drop method. Micro methods based on Harrison's work (1947) were used. Hæmoglobin and hæmatocrit readings were by the Sahli and Wintrobe methods respectively.

Clinical Pattern of Nine Children with Potassium Deficiency Alone.

The sequence of events in cases of this group was one of continued potassium loss from severe diarrhœa and a poor oral intake of milk over several weeks, a failure to improve with a steady weight loss over this period, then a rapid and often sudden collapse when the potassium depletion reached a critical level, and finally a rapid response to potassium therapy.

All of these children had been ill for some time, twelve days being the shortest time and six weeks the longest. The diarrhœa was very persistent in all cases, and vomiting occurred in most of them. Intravenous administration of sodium chloride, glucose and water was necessary to maintain an adequate fluid intake in seven of the nine, as vomiting or great difficulty with feeding prevented an adequate oral intake. Often a sick, dehydrated infant would temporarily improve with intravenous therapy and then relapse because the oral intake of water, sodium chloride and milk was inadequate. Further intravenous therapy, usually with N/4 sodium chloride solution in 5% glucose in water, would bring improvement, but this improvement was often not maintained and the infant would still look ill. Weight was usually lost steadily despite adequate water, salt and sugar intake, and by some even when the milk intake seemed adequate. The outstanding clinical feature leading up to the critical phase of potassium depletion was severe persistent diarrhœa over some weeks, together with difficulty in the giving of sufficient fluid and milk by mouth so that repeated intravenous therapy became necessary.

Potassium deficiency was declared clinically by a relatively sudden collapse, although it was evident that the infant was sick for some days prior to the collapse. The most characteristic clinical symptom seemed to be a state of extreme apathy and weakness, which developed usually over a few hours. After this the infant often lapsed into a state of either semiconsciousness or unconsciousness. In this state of extreme apathy minor surgical procedures, such as the exposure of a vein, could be accomplished without the use of any anæsthetic, the baby making no cry or movement. The limbs were limp, the hypotonia was extreme and resembled that seen in patients with severe pink disease. The deep tendon reflexes were absent. Often the eyes looked sunken, with dark shadows around them, the skin and subcutaneous tissue were inelastic and had obviously lost substance. In contradistinction, the tongue and mouth were usually moist and the infant was passing urine in adequate amounts. The lips and extremities were usually slightly cyanosed and felt cold, and the capillary circulation was very sluggish, the blood returning very slowly after squeezing of the finger or ears. The pulse was weak, thready and rapid (140 to 160 beats per minute), the blood pressure was low, and heart sounds were feeble. The abdomen was usually distended with fluid and gas, and in some patients a "ladder" pattern was observed. Often the diarrhœa was very watery, and watery bile-stained fluid seemed to flow out of the mouth without the effort of vomiting, a state clinically resembling that of gastric dilatation. Respirations were shallow and irregular, often with periods of apnœa.

Estimation of serum electrolyte levels of potassium showed figures ranging from 1·7 milliequivalents per litre to 3·1 milliequivalents per litre, the average figure being 2·5 milliequivalents per litre. Electrolyte levels of sodium, chloride, bicarbonate and protein were within the normal range in all but two patients, who had mild hypo-osmolarity, the sodium and chloride levels both being reduced by approximately 15 to 20 milliosmols. Electrocardiograms were prepared from only four patients, and surprisingly only one showed characteristic changes of a prolonged *Q-T* interval, depressed *S-T* segment and inverted *T* waves. In the other three minor non-specific changes were seen in the *T* waves in the form of low amplitude waves.

Improvement with potassium therapy often occurred as rapidly as the collapse developed. In some the response was quite out of proportion to the amount of potassium administered; in a few patients the clinical condition had improved dramatically within half to one hour. Response was noted from the improved circulation, the disappearance of cyanosis, and the recovery from extreme apathy or state of unconsciousness. The infants looked better and would show spontaneous movements, and usually the deep reflexes would return in twelve to twenty-four hours. In some patients the abdominal distension disappeared rapidly, the vomiting ceased and the diarrhœa was greatly reduced from as many as 12 motions *per diem* to three within twenty-four hours. These nine patients all recovered. In seven of the nine cases potassium was administered intravenously as potassium chloride with, in most cases, the addition of potassium dihydrogen phosphate. All patients were given potassium orally, usually in the form of potassium citrate, and in two this was the sole method of treatment. Potassium therapy was continued until full milk feedings were resumed.

Two case histories serve to illustrate some of these clinical features in detail. The first patient developed potassium deficiency from diarrhœa which had persisted for five weeks and from a defective oral intake of milk over a period of six days. The clinical features of collapse with a low serum potassium level and the rapid response to potassium therapy are typical.

A healthy male infant, with a birth weight of six pounds three ounces and three weeks premature, developed diarrhœa at the age of two weeks. After five days' illness he was admitted to the Children's Hospital on May 7, 1951, weighing five and three-quarter pounds. He was a vigorous baby and did not seem seriously ill. He passed five or six stools daily, some containing mucus with streaks of blood, but culture of these stools did not reveal the presence of any pathogenic organisms. After a short period of starvation, during which time adequate quantities of N/4 sodium chloride solution in 5% glucose in water were given orally, he took very well a feeding of equal parts of skimmed milk and water with added sugar. He improved rapidly and gained one pound in weight in two weeks, and as his mother seemed competent to manage him, he was allowed to go home after two weeks in hospital, although he was still having three or four loose stools *per diem*. Soon after he went home his diarrhœa recurred, he commenced vomiting, lost weight, and was readmitted to hospital on May 26, twenty-four days after the diarrhœa commenced. He was still a vigorous baby, with a temperature of 98·4° F., a pulse rate of 132

per minute, and a respiration rate of 30 per minute. He had, however, lost half a pound in weight and now weighed six and a quarter pounds. The diarrhœa and vomiting persisted, with five or six loose watery stools and three or four vomits each day. On the fourth day after admission he had lost more weight and looked dehydrated, so intravenous therapy was commenced with N/4 sodium chloride solution with 5% glucose solution. Serum electrolyte values on this day were: potassium five milliequivalents per litre, sodium 135 milliequivalents per litre, chloride 105 milliequivalents per litre, bicarbonate 18 milliequivalents per litre and protein 16 milliequivalents per litre. The hæmoglobin value was 14 grammes per 100 millilitres and the hæmatocrit reading 44%. He improved rapidly over the next forty-eight hours, but still vomited, and his oral intake of milk was poor. On the following day, thirty days after the diarrhœa commenced, he looked pale and ill, was slightly cyanosed, very listless and apathetic, and refused to suck. He had lost more weight and now weighed five and three-quarter pounds. His abdomen was distended, his respirations were shallow and irregular, his pulse was weak, thready and rapid. Serum electrolyte values were: potassium 2·9 milliequivalents per litre, sodium 139 milliequivalents per litre, chloride 103 milliequivalents per litre, bicarbonate 23 milliequivalents per litre, and protein 14 milliequivalents per litre. The hæmoglobin value was 11 grammes per 100 millilitres and the hæmatocrit reading 35%. Potassium therapy was commenced by giving 1·0 gramme of potassium chloride and 1·0 gramme of potassium dihydrogen phosphate per litre of N/4 sodium chloride solution in 5% glucose solution at the rate of 30 millilitres per hour. By the end of 12 hours the infant had improved very considerably, the colour was good, and he was no longer apathetic and would suck well. Potassium citrate, three grammes daily, was now given orally. The vomiting ceased and the abdominal distension became less, and by the end of twenty-four hours the baby's condition was very satisfactory. The following day the diarrhœa was greatly reduced (three stools in twenty-four hours). Intravenous therapy was gradually discontinued over a period of three days after the collapse, as the infant was taking fluid and milk by mouth very well. Convalescence was entirely uneventful, and the baby gained weight rapidly and was sent home on June 11, five and a half weeks after the illness commenced, and weighing seven and three-quarter pounds—a gain of two pounds. Serum electrolyte figures a week after the collapse from potassium deficiency were: potassium six milliequivalents per litre, sodium 132 milliequivalents per litre, and chloride 94 milliequivalents per litre.

The second patient illustrates how potassium deficiency may develop from persistent diarrhœa even though the intake of milk is adequate.

A male infant, aged seven months, developed diarrhœa on a migrant ship five weeks before admission to the Children's Hospital on November 8, 1950. During this time there had been little or no vomiting but persistent diarrhœa of moderate degree, and milk had been taken reluctantly. On admission to hospital he was an alert, playful baby with reasonable tissue turgor and did not seem ill. His weight was seventeen and a half pounds. He took well his feedings of sweetened condensed milk (one part to six and a half parts of water), the total intake being 40 ounces per day. He had an occasional small vomit and passed five or six loose stools daily, culture of which did not yield any pathogenic organisms. He had a low-grade increase of temperature (100° F. *per rectum*) each evening. For the first five days in hospital he seemed well but continued to lose weight despite this adequate milk intake. On the sixth day he became pale and did not look so well, and he did not take feedings well. On the seventh day he became extremely listless and very hypotonic and appeared semiconscious with his eyes turned up. He would not suck, and the deep reflexes could not be elicited, whereas on his admission to hospital they were quite active. The tongue was moist and he was passing adequate quantities of urine. The respirations were shallow and irregular, and the rate was 34 per minute. The lips and eyes and fingers were slightly cyanosed, the capillary circulation was poor, and the pulse was weak and thready, with a rate of 150 per minute. The abdomen was distended. Serum electrolyte levels were: potassium 2·8 milliequivalents per litre, sodium 139 milliequivalents per litre, chloride 101 milliequivalents per litre, bicarbonate 26 milliequivalents per litre, and protein 16 milliequivalents per litre. The hæmoglobin value was 14 grammes per 100 millilitres and the hæmatocrit reading 47%. Treatment was given intravenously with N/4 sodium chloride solution in 5% glucose solution, to which were added 1·0 gramme of potassium chloride and 1·0 gramme of potassium dihydrogen phosphate per litre, and the child rapidly commenced to improve. He was also given potassium citrate, six grammes orally daily, for two days. Over the next two and a half days he was given 2500 millilitres of N/4 sodium chloride solution with added potassium chloride and potassium phosphate, one gramme of each to the litre. At the end of this time he was extremely well, of good colour, bright and active, and sitting up and playing. His abdominal distension disappeared, and his diarrhœa almost ceased, for he passed only one or two motions daily. His weight, which had fallen to 17 pounds at the time of the collapse, steadily rose, and he gained one pound two ounces in the next two weeks. He was discharged from hospital on December 3, clinically well and having been in hospital for twenty-one days. Two days after the commencement of potassium therapy the serum potassium level was 4·1 milliequivalents per litre, the sodium level 136 milliequivalents per litre, the chloride level 106 milliequivalents per litre, the bicarbonate level 23 milliequivalents per litre and the protein level 15 milliequivalents per litre. The hæmoglobin value was now 12 grammes per 100 millilitres and the hæmatocrit reading 37%. Just prior to his being sent home his serum potassium level was 5·0 milliequivalents per litre.

This infant is an unusual example of potassium deficiency, in that despite a good and adequate intake of milk by mouth and minimal or no vomiting, he developed a severe degree of potassium deficiency. However, he had had moderately severe diarrhœa for a period of six weeks. The clinical features of long-continued diarrhœa, loss of weight despite an adequate caloric intake, collapse with pronounced apathy, semi-coma and flaccidity, low serum potassium level and rapid response to potassium leave no doubt that hypokalæmia was the cause of his collapse.

One other patient of the nine resembled this patient in clinical features and despite an adequate and normal milk intake developed chronic potassium deficiency. One can assume only that the loss by the stool and urine must have been greater than the intake and absorption from the milk, which contains a very considerable quantity of potassium.

Potassium Deficiency Associated with Infections.

Four patients developed potassium deficiency and at the same time had an infection; in three the infection was bronchopneumonia, in one pyelonephritis, and two of these patients also had liver damage. It was impossible with these patients, who were extremely ill with features of circulatory and respiratory embarrassment and toxæmia, to state specifically that the symptoms and signs they showed were solely due to potassium deficiency. In the other group of nine patients, with the exception of two patients who had a low serum sodium and chloride content, the electrolyte pattern was normal apart from the low serum potassium content, and there was no evidence of any additional complication, such as an infection or disordered liver function. The rapid response, often within a few hours or even less, to potassium administration is strong evidence that this was the sole factor causing the symptoms of collapse. In these four patients the added complicating factor of infection and liver damage clouded the picture, and although these patients had a very low serum potassium level and improved with potassium therapy, it was not possible to be so definite that their symptoms and signs were due entirely to hypokalæmia. Of these four patients, three died and one recovered. A case history serves to illustrate some of these points.

A female infant, aged seven months, was admitted to the Children's Hospital on December 23, 1950, having been ill for two weeks with diarrhœa and vomiting and a chest infection. She was a sick, dehydrated baby, weighing twelve pounds two ounces. She had a temperature of 100° F., a pulse rate of 160 per minute and a respiration rate of 28 per minute. Although clinical examination of the chest gave normal results, X-ray examination showed an area of inflammation in the right side of the chest in the axillary region, so that chemotherapy with penicillin and streptomycin was commenced. Intravenous therapy with N/4 sodium chloride solution in 5% glucose in water was commenced, and the child improved very considerably over a period of twenty-four hours. During this time the child was given sips of N/4 sodium chloride solution and 5% glucose in water. In thirty-six hours, as the child seemed well, sweetened condensed milk, one part to eight parts of water, was given (two ounces two-hourly). She took this well for thirty-six hours and then refused feedings, so an intragastric drip of this milk mixture was commenced. However, she began to vomit, and the diarrhœa was so profuse that intravenous

administration of N/4 saline in 5% glucose solution was recommenced. During the period of the twelve days after admission to hospital the diarrhœa persisted, six to eight large watery stools being passed each day; the child vomited intermittently and took only small amounts of sweetened condensed milk mixture by mouth or gastric drip administration. On some days the oral intake was 20 ounces, on other days as low as 10 ounces. Some N/4 saline in 5% glucose solution was given by mouth, but intravenous therapy with N/4 saline in 5% glucose solution was necessary to supply adequate water to the child. The pattern of severe diarrhœa, deficient oral intake of milk and intravenous administration of water and salt during most of the twelve days clearly sets the stage for collapse from severe potassium depletion.

At this stage the child was ill and not doing well, and further X-ray and clinical examination showed that the area of inflammation in the right side of the chest had not responded to penicillin and streptomycin therapy. As an empyema was suspected, this inflammatory area was needled, but no pus was obtained. On the thirteenth day the child became very limp and listless and would hardly suck. The abdomen was distended, and green fluid drooled from the mouth. The deep reflexes were absent. The pulse had a rate of 160 per minute and was weak and thready; the lips, ears and fingers were slightly cyanosed, with a poor capillary circulation. The liver was now enlarged to two and a half fingers' breadth below the right costal margin. At this stage the serum electrolyte pattern showed the following values: sodium 130 milliequivalents per litre, potassium 1·9 milliequivalents per litre, chloride 94 milliequivalents per litre, bicarbonate 29 milliequivalents per litre, and protein 12 milliequivalents per litre. The problem was a considerable one, as the child had gross hypokalæmia, pneumonia and probably toxic hepatitis.

Potassium therapy, two grammes of potassium chloride in one litre of N/4 saline in 5% glucose solution, was commenced, and 1000 millilitres were given in twenty-four hours. Improvement occurred, but it was not dramatic as in other patients. Potassium chloride, approximately two grammes daily, was given intravenously, and three grammes of potassium citrate were given orally over the next three days. On the sixteenth day the child was much better and was taking feedings well, and the serum electrolyte values were now as follows: potassium 3·0 milliequivalents per litre, sodium 125 milliequivalents per litre, serum chloride 91 milliequivalents per litre, bicarbonate 30 milliequivalents per litre and protein 12 milliequivalents per litre. Oral potassium therapy was continued. On the eighteenth day the child was even further improved; she was taking feedings fairly well, would follow objects with her eyes, and had a good cry, and the deep reflexes were active. This picture was in marked contrast to that of the limp, listless baby who would give no response to any painful stimulus. Serum electrolyte values at this stage showed mild hypoosmolarity: potassium 5·3 milliequivalents per litre, sodium 131 milliequivalents per litre, chloride 94 milliequivalents per litre, bicarbonate 22 milliequivalents per litre, and protein 12 milliequivalents per litre.

Over the next six days the child's condition slowly deteriorated, despite the continued use of potassium. At first feedings were taken well by mouth, and then vomiting recurred and intravenous therapy was necessary. The clinical signs of pneumonia persisted on the right side, the liver became larger, and the diarrhœa was profuse. The child died on the twenty-fourth day after admission to hospital. Post-mortem examination showed a wasted baby with a small loculated empyema containing one ounce of thick yellow pus in the axillary region of the right pleural cavity and patchy bronchopneumonia of the right lung. The ileum and colon were œdematous and the mucosa was engorged but no actual ulceration was present. The liver was enlarged and a gross diffuse fatty vacuolation was present. Both middle ear cavities contained thick yellow pus.

This baby presented at hospital with features of entero-colitis and pneumonia, and owing to severe diarrhœa and defective intake of milk by mouth chronic potassium depletion occurred by the thirteenth day. This showed a slow but steady and definite response to potassium therapy over a period of five days, but thereafter gradually the child became exhausted and died of respiratory sepsis and liver damage by the twenty-fourth day. It is possible that the respiratory suppuration and liver damage were factors in preventing a rapid response to potassium therapy.

Discussion.

A study of the nine patients gives the clinical pattern of moderately severe uncomplicated potassium deficiency. The evidence submitted that these nine infants had chronic potassium deficiency is, firstly, that there was long-continued potassium loss from persistent diarrhœa and an inadequate intake of potassium owing to a poor milk intake in the majority of the cases. Secondly, they developed symptoms of collapse which were similar to those occurring in chronic potassium deficiency in adults and experimental animals. Thirdly, with no other change in treatment than the administration of potassium a rapid alleviation of their symptoms occurred. Fourthly, the serum potassium level was low and rose after the administration of large amounts of potassium, and in some cases did not return to normal until a number of days had elapsed. It is clearly understood that a low serum potassium value alone is not proof of chronic intracellular potassium deficiency. Balance studies demonstrating that potassium is retained considerably in excess of the retained nitrogen are theoretically necessary to prove chronic potassium deficiency, but it was not practical to carry out the studies in these patients. However, the evidence submitted does not seem to leave reasonable doubt as to the diagnosis.

A very interesting clinical observation is the considerable and rapid relief of vomiting, diarrhœa and abdominal distension following the administration of potassium. This occurs experimentally in potassium-deficient animals (Webster, 1950), and it is probable that this is the explanation in some of these infants.

The practising clinician who has to care for sick infants with entero-colitis wants to know whether there is a clear-cut clinical pattern of chronic potassium deficiency with a diagnostic group of signs and symptoms. The answer is no, for this clinical picture of extreme apathy, listlessness, severe hypotonia with absent deep reflexes, poor peripheral circulation, and abdominal distension, may be common not only to potassium deficiency but to the circulatory failure and toxæmia due to any severe infection or to other severe disturbances of water and electrolyte metabolism. Any infant ill with entero-colitis who develops an infection, whether bronchopneumonia, pyelonephritis, pyæmia or peritonitis, may present a very similar clinical pattern. A severe hypotonic type of dehydration with circulatory failure, the result of inadequate sodium intake or excessive sodium loss, may closely resemble the clinical picture of hypokalæmia.

However, the diagnosis will be strongly suggested by a consideration of the events preceding this collapsed state. A history of one or several weeks' continued diarrhœa with defective intake of potassium in the form of milk, often together with the intravenous administration of large doses of sodium, certainly means that chronic depletion of cell potassium has occurred. Circulatory collapse due to infection can be eliminated only by a very careful clinical examination of the patient, microscopic examination of the urine and X-ray examination of the chest. The fact that adequate amounts of water, sodium and chloride have been supplied either orally or intravenously makes it highly improbable that any collapse or symptoms are the result of severe sodium depletion with dehydration. If infection and other electrolyte disturbances can be eliminated then it is probable that hypokalæmia is the cause. A low serum potassium level with a normal serum electrolyte pattern for sodium, chloride, bicarbonate, calcium and protein is strong evidence for the diagnosis. A rapid alleviation of the signs and symptoms of collapse following the administration of potassium makes the diagnosis almost certain. Electrocardiographic evidence has been very variable; of four patients, three showed no diagnostic changes and one showed typically a low take-off of the *ST* segment, an inverted *T* wave and a prolonged *Q-T* interval. These changes disappeared after potassium therapy.

Treatment of the chronically potassium-depleted infant requires time to replace potassium, so that administration must be continued for some days. Provided the child has been receiving adequate amounts of water and is passing adequate amounts of urine then it is quite safe to administer potassium at once. Potassium chloride, one gramme, or a mixture of half a gramme of potassium chloride and half a gramme of potassium dihydrogen phos-

phate to 500 or 1000 millilitres of N/4 sodium chloride solution with 5% glucose solution was given intravenously to most of these patients. For the small babies under ten pounds in weight the solution was used containing one gramme of potassium per litre, for the larger babies the solution containing two grammes to the litre. It is quite safe to administer these solutions up to a rate of 100 millilitres per pound of body weight *per diem* if necessary. Oral potassium therapy was also given as soon as the infant could take fluid orally, usually in the form of potassium citrate, two to four grammes daily in divided doses according to the size of the infant. Intravenous therapy was usually discontinued in thirty-six to seventy-two hours, but the oral potassium therapy was continued until the child was taking full caloric requirements daily in the form of milk.

Prevention of potassium deficiency will occur only when the disordered physiology of entero-colitis is understood by the clinician caring for the patient. The infant with severe persistent diarrhœa is steadily depleting his body store of potassium, and this loss must be made good. Govan and Darrow (1946), Butler and others (1946), and Flett and others (1949) have shown that replacement of the potassium loss is necessary in the treatment of infants with entero-colitis. Govan and Darrow (1946) have claimed an extensive reduction in the mortality rate with the routine use of potassium in all patients with diarrhœa, but their clinical experiment was not controlled adequately. It is very probable that it is only the infant who remains sick for some time in whom the potassium becomes so depleted that serious symptoms develop. The body has very considerable reserves of potassium, and as the average patient with entero-colitis can take milk feedings fairly soon, the routine administration of potassium to all infants with entero-colitis would seem unnecessary. The fact that oral milk feeding has been resumed early in our own hospital is probably the important factor in determining why serious potassium deficiency is not a common problem, for there were only 13 cases in a series of 496 sick infants.

However, it must be appreciated that the group of patients in whom the diarrhœa is severe and persistent, and who often vomit or have difficulty in taking adequate quantities of fluid and milk by mouth, are in grave danger of developing severe potassium deficiency. The potassium losses in this group are not adequately replaced by the limited milk intake, so that in time a serious state of depletion occurs. It is this group of patients who require potassium therapy, so as to prevent depletion from reaching a stage at which serious symptoms will arise. A simple method of prevention, and one that is now in use at the hospital, follows the principles laid down by Butler (1946). A solution containing 32 milliequivalents per litre of potassium, 50 milliequivalents per litre of sodium, 40 milliequivalents per litre of chloride, and 10 milliequivalents per litre of phosphate in 5% glucose and water is administered orally to all children with severe entero-colitis as soon as they can absorb fluid by mouth and is continued in decreasing amounts until full-strength milk feedings are resumed. If the infant has had severe diarrhœa for five or six days or longer before admission to hospital and requires intravenous therapy, then it is wise to administer potassium intravenously pending oral administration of potassium to the child. A solution of N/4 sodium chloride with one gramme of potassium chloride, or a solution with sodium lactate, sodium chloride and potassium chloride to give approximately 40 milliequivalents per litre of sodium, 20 milliequivalents per litre of potassium and 30 milliequivalents per litre of chloride supplies this need well.

Summary.

1. The clinical manifestations of potassium deficiency in 13 children in a series of 496 infants with entero-colitis are described.

2. The diagnosis, treatment and prevention of this condition are discussed.

References.

Butler, A. M., Talbot, N. B., Crawford, J. D., MacLachlan, E. A., and Appleton, J. (1946), "Parenteral Fluid Therapy in Diarrhœal Disease", *American Journal of Diseases of Children*, Volume LXXII, page 481.

Darrow, D. C. (1946), "The Retention of Electrolyte during Recovery from Severe Dehydration due to Diarrhœa", *The Journal of Pediatrics*, Volume XXVIII, page 515.

———, Pratt, E. L., Plett, J., Gamble, A. H., and Wiese, H. F. (1949), "Disturbances of Water and Electrolytes in Infantile Diarrhœa", *Pediatrics*, Volume III, page 129.

Flett, J., Pratt, E. L., and Darrow, D. C. (1949), "Methods Used in Treatment of Diarrhœa with Potassium and Sodium Salts", *Pediatrics*, Volume IV, page 604.

Gamble, J. L. (1950), "Chemical Anatomy, Physiology and Pathology of Extracellular Fluid", Harvard University Press, Cambridge, 1950, chapter 40-B.

Govan, C. D., and Darrow, D. C. (1946), "The Use of Potassium Chloride in the Treatment of the Dehydration of Diarrhœa in Infants", *The Journal of Pediatrics*, Volume XXVIII, page 541.

Harrison, G. A. (1947), "Chemical Methods in Clinical Medicine", Third Edition.

Rapoport, S., Dodd, N., Clark, M., and Sylim, I. (1947), "Post-Acidotic State of Infantile Diarrhœa; Symptoms and Chemical Data", *American Journal of Diseases of Children*, Volume LXXIII, page 391.

Webster, D. R., Henrikson, H. W., and Currie, D. J. (1950), "The Effect of Potassium Deficiency on Intestinal Motility and Gastric Secretion", *Annals of Surgery*, Volume CXXXII, page 779.

SOME ASPECTS OF PRE-ECLAMPSIA AND ECLAMPSIA.[1]

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IN the efforts to discover the ultimate cause of pre-eclampsia with its possible climax of eclampsia, much work has been done on the hæmodynamics of pregnancy.

Recent trends in research have tended to show that interference with the blood supply of the uterus may produce interference with the nutrition of the placenta, thus releasing substances into the blood-stream which may in themselves be toxic or may alter the physiological endocrine balance of the body.

Work on cardiac output in normal pregnancy by Palmer and Walker (1949) and by Hamilton (1949) has shown that there is a progressive increase from the earliest weeks until the last eight weeks, when there is a gradual fall. The mean cardiac output in normal pregnancy is 5·8 litres per minute, as opposed to 4·6 litres per minute in the non-pregnant state.

There is no known method of measuring uterine blood flow in the human uterus; but Kellar (1950) has estimated that at the moment of maximum cardiac output and blood volume, the uterine blood flow is probably not more than one litre per minute. The obvious inference is that this amount would be altered by the mechanisms operating in diseased states and in adiposity.

A study of the peripheral blood flow through the muscles and skin in the toxæmias of pregnancy was undertaken by Burt (1950), who found that when compared with that of a control group of non-pregnant women, the blood flow through the upper extremity in women suffering from pre-eclampsia and hypertension complicated by pregnancy was approximately twice as great as in the non-pregnant state. This increase is greater than that observed in the normal pregnant patient.

Whilst the fact is accepted that the ætiology of pre-eclampsia is still unknown, it is nevertheless possible to modify the course and incidence of the disease.

At the Women's Hospital, Crown Street, Sydney, there have been, up to the time of preparation of this paper, 6560 consecutive "booked" confinements without a single case of eclampsia. This almost unbelievable result has been achieved by the concerted efforts of the honorary medical staff, the medical superintendent, the resident medical staff, the sisters, the dietitians and the almoners. The results obtained are due to the hospital staff as a whole; but I should particularly like to mention the untiring vigilance

[1] Presidential address delivered to the Section of Obstetrics and Gynæcology of the New South Wales Branch of the British Medical Association on November 21, 1951.

of the medical superintendent, Dr. R. J. Hamlin, in carrying out the details involved.

There is now in progress a drive, which we think is being successful, to lessen the number of cases of pre-eclampsia.

Bastiaanse and Mastboom (1949), quoted by Greenhill, report that despite all precautions, eclampsia developed in 17 cases (0·055%) out of 29,130 pregnancies between 1938 and 1948 at Wilhelmina Hospital, Amsterdam. Their ante-natal care included determination of weight, of blood pressure, of pre-tibial œdema, of urinary albumin content, and of sodium chloride content of the urine when a saltless diet had been prescribed. If we are to judge by these figures, there should now have been at least four cases of eclampsia at the Women's Hospital, Crown Street, Sydney.

Part of this paper describes how the results mentioned earlier have been achieved, and what is being done at present, thus providing you with material for thought and criticism.

The claim is made that by adequate ante-natal care eclampsia may be prevented, and that the incidence of severe pre-eclampsia may be lessened. No claim is made that pre-eclampsia is preventible. Patients with multiple pregnancy, hydatidiform mole and hydramnios still sometimes develop severe pre-eclampsia.

Attention was at first paid chiefly to developing a routine which would give the earliest possible indication that pre-eclampsia was commencing, or had commenced; but very soon efforts were directed also to the development of methods which would reduce the number of pre-eclamptic cases, and which would lessen the severity of the disease in those cases in which it was not possible to prevent it.

Pre-eclampsia is preeminently a disease of signs. By the time symptoms appear the entity is well established.

DETECTION.

The members of the out-patient staff are constantly on the watch for the first indication of pre-eclampsia. Patients whose condition arouses suspicion are asked to report back in a few days, while those with more definite indications are recommended for admission to hospital.

The out-patient cards of all ante-natal patients who attend that day are sent to the medical superintendent's office each evening, where they are checked to see that patients return when they are asked to do so. Should a patient not report back on the date stipulated, she is interviewed by the almoner's department, and if necessary visited by one of the resident medical staff. It is no excuse to say that a patient developed severe pre-eclampsia because she did not return to the out-patient department. The onus is on the hospital to see that she does return. Early detection is achieved by observations of weight, œdema, blood pressure and urine.

Weight.

Women who are overweight at the beginning of pregnancy are the most prone to develop pre-eclampsia.

A detailed study of the out-patient records of 500 consecutive normal patients reveals that there were 144 women who weighed over nine stone seven pounds at the beginning of their pregnancies, and 356 women who weighed under nine stone seven pounds at the beginning of their pregnancies. Of the 144 women who weighed over nine stone seven pounds at the beginning of pregnancy, 115 (80%) developed signs of pre-eclampsia as evidenced by bilateral clinical œdema of the feet or hands or varying degrees of generalized œdema, a rise in blood pressure of at least 20 millimetres of mercury in either systolic or diastolic readings, a blood pressure reading of over 140 millimetres of mercury, systolic, or 90 millimetres, diastolic, or varying amounts of albumin in the urine. On the other hand, of the 356 women who weighed under nine stone seven pounds at the beginning of their pregnancies, 172 (48·3%) developed signs of pre-eclampsia.

A gain of over four pounds in any one month of pregnancy is regarded as an indication for closer observation and investigation; but if the gain is over four pounds per month on any two separate months, pre-eclampsia is usually inevitable, and such patients are either admitted to the hospital for observation and treatment or put on to a reducing diet and asked to return in one week.

Of 419 pre-eclamptic patients, booked before the twentieth week and later admitted to the hospital during the twelve months ended June 30, 1951, there were 213 patients who weighed under nine stone seven pounds at the beginning of their respective pregnancies and 206 who weighed over nine stone seven pounds.

Of the 213 patients whose weight was under nine stone seven pounds, 173 (81·22%) either gained an excessive amount of weight during the whole pregnancy or their rate of gain was excessive for a minimum period of six weeks.

Of the 206 patients who weighed over nine stone seven pounds, only 76 (36·89%) gained too much weight, either during the whole pregnancy or for a minimum period of six weeks; but yet there was a nearly equal number of pre-eclamptics from these two groups of patients.

Of these pre-eclamptic subjects, 94% showed a gain at the rate of over four pounds per month for a minimum period of six weeks or were overweight to start with.

An analysis of these results indicates that in women of normal weight an excess gain is a predisposing factor to pre-eclampsia, while in women of excessive weight there appears to be some factor present which predisposes them to pre-eclampsia even if their weight is strictly controlled throughout pregnancy. This obesity factor may be a breakdown in the functions of the liver or kidney, rendered evident by the added physiological test of pregnancy, or it may be an endocrine factor which predisposes the subject to both excess weight and pre-eclampsia. Whatever the answer, it becomes apparent that dietary control of weight is the only measure available to counteract it.

It is considered that the optimum gain for a patient who is of normal weight at the onset of her pregnancy is 21 to 24 pounds.

Women who are very obese should have their weight reduced as much as possible during their pregnancies.

Œdema.

All patients with bilateral peripheral œdema or with generalized œdema are regarded as showing evidence of pre-eclampsia until proof to the contrary is obtained. Such patients are given a salt-free diet of approximately 1750 Calories, and are advised to rest as much as possible. If there is no improvement in one week, admission to hospital is arranged for.

All patients with severe œdema are admitted to hospital forthwith for investigation and complete bed rest.

Blood Pressure.

Patients having a systolic blood pressure reading of over 140 millimetres of mercury, or a diastolic reading of over 90 millimetres of mercury, are regarded as showing evidence of pre-eclampsia. In addition to these standard limits of blood pressure, great notice is taken of a progressive rise in blood pressure, irrespective of the actual figures recorded.

The relativity of blood pressure in pre-eclampsia was fully and ably discussed by T. Dixon Hughes in a paper read during the Inaugural Congress of the Royal College of Obstetricians and Gynæcologists held in Sydney during March, 1951. As an example, a patient with a blood pressure of 130 millimetres of mercury, systolic, and 90 millimetres, diastolic, who had started her pregnancy with readings of 100 millimetres of mercury, systolic, and 60 millimetres, diastolic, would be in far greater danger of developing eclampsia than a patient with blood pressure readings of 150 millimetres of mercury, systolic, and 100 millimetres, diastolic, who had started her pregnancy with readings of 140 millimetres of mercury, systolic, and 90 millimetres, diastolic.

Mukherjee and Govan (1950) have demonstrated the importance of the diastolic blood pressure readings in cases of pre-eclampsia. They state that the hypertension of pre-eclampsia is primarily diastolic in origin, and that as the condition develops the increase in diastolic pressure occurs in advance of, and is greater than, the increase in systolic pressure.

In our patients a very strict watch is kept for rises in the diastolic blood pressure.

Albuminuria.

Patients showing albuminuria in any quantity other than a trace are admitted to hospital for observation and treatment.

Warning Signs.

In the earlier days we regarded albuminuria as the first sign of pre-eclampsia. Then we moved our attention to the blood pressure readings. As time went on we became conscious of the significance of œdema, and now we look to the weight records to give us the first warning of impending pre-eclampsia.

TREATMENT.

Immediately one, some or all of the signs enumerated have been detected, treatment is instituted. Diet and rest constitute the major factors in treatment.

If the signs are mild, the patient is given a diet of low salt content and of approximately 2100 Calories, and is advised to rest for about half of each day. If she is overweight, the Calories are reduced to approximately 1750 (reducing diet). She is instructed to return to the out-patient department within three to seven days according to the severity of the signs. If there has not been a decided improvement when she returns, the patient is recommended for admission to hospital.

If any of the signs of pre-eclampsia are at all pronounced, the patient is recommended for admission to hospital without any period of home treatment. After her admission to hospital the patient is given a diet of low salt and moderate protein content and of approximately 2100 Calories, and is kept at rest in bed. Overweight patients have fewer Calories (1900 or 1750), and the very obese have only about 1100 Calories per day for a few days or more.

In the extremely severe cases, now found only amongst "unbooked" patients, the subjects are kept on fluids only for twenty-four or forty-eight hours; sometimes the fluid is given by the intravenous route, but great care is taken not to give more than 500 millilitres of dextrose solution to any œdematous patient who is oliguric or anuric. In these cases the peanut oil and glucose regime of Bull, Bywaters and Joekes (1950) is instituted. (All diet sheets mentioned are appended to this paper.)

PREVENTION.

The factors of prevention are diet, weight control, rest, and the prevention or treatment of anæmia. Weight control is, of course, dependent upon diet. As it is recognized that diet plays such an important role in the treatment of pre-eclampsia, it is logical to conclude that a correct diet throughout pregnancy will play a large part in the prevention of pre-eclampsia.

The Diet.

A correct diet for pregnancy must provide sufficient Calories for the needs of the mother and the fœtus. It must be a balanced diet, containing a liberal supply of protein, minerals and vitamins, and a sufficient supply of carbohydrate and fat.

Protein.

Nitrogen storage commences as early as the tenth week of pregnancy. Large amounts of nutritive factors are stored by nitrogen retention. It has been estimated that the total gain in nitrogen storage during pregnancy varies between 200 and 400 grammes (P. F. Williams, 1945). A diet rich in protein is necessary for this storage to occur. Protein, together with iron in the diet, maintains an adequate hæmoglobin level. A diet adequate in protein is usually found to be adequate in iron.

Dogs rendered anæmic by repeated bleedings quickly regenerate hæmoglobin when fed on meat, but do not do so when fed on carbohydrate (Best and Taylor, 1945). Protein greatly increases the absorption of available calcium (R. A. McCance, 1942). Protein lessens the incidence of toxæmia. W. T. Tompkins (1941) found that the incidence of pre-eclampsia was four times greater among women who had a diet of their own choosing than it was among women who received a balanced diet containing 110 grammes of protein.

The report of the Committee of Inquiry into the Medical Aspects of the Decline of the Birth Rate, published by the National Health and Medical Research Council (1948), states that among 110 multiparous women whose diet was adequate not one patient developed toxæmia, whereas the incidence of toxæmia in a control group of women was 14%. The diet was considered adequate if it contained at least 45 grammes of animal protein, together with sufficient calcium, vitamin B_1 and vitamin *C*.

The diet must contain at least 1·5 grammes and preferably 2·0 grammes of protein per kilogram of body weight.

The National Research Council recommends a minimum of 85 grammes of protein daily, of which at least 45 grammes must be animal protein.

Calcium.

The daily diet must contain at least 1·5 grammes of calcium. It should be remembered that cereals and wholemeal bread contain phytin, which depresses calcium absorption.

Sodium Chloride.

The approximate daily requirement of salt is four grammes. In this respect it is interesting to note that the average daily salt intake in random diets is 10 grammes. In ordinary diets without salt added at the table the intake is six grammes.

In a diet containing foods of low salt content prepared and cooked without salt, the intake is two grammes. This is the level reached in most salt-free diets prescribed during pregnancy.

In a diet chosen from foods with the lowest possible salt content, prepared and cooked without salt, the intake is 0·5 gramme. Such a diet is exemplified by the rice, eggs and milk diet described by Mayes (1950).

Vitamins.

Of thiamine 1·8 milligrammes and of ascorbic acid 100 milligrammes are required daily.

A diet containing approximately 2400 Calories and embodying the above principles, may be easily attained by advising the patient to have each day two liberal helpings of lean meat, one or two eggs, one pint of milk, two ounces of cheese, three ounces of bread (two slices), three pieces of fruit, average helpings of vegetables, one ounce of butter, one ounce of sugar, half an ounce of jam, little added salt, and no bicarbonate of soda.

The printed diet sheet given to normal pregnancy patients is shown in the appendix.

Weight Control.

The total weight gain for the whole of pregnancy as previously stated must not be more than 21 to 24 pounds.

The increased body weight brought about by changes in the uterus, breasts and blood volume does not manifest itself before the twelfth week of pregnancy. The gain in the first three months should therefore be limited to one pound. The rate of gain from this point onwards should be limited to a maximum of four pounds in any one month until the last month, when only three pounds should be

allowed. Should the gain in any one month exceed four pounds, the amount of all articles of diet except the animal protein is reduced until the rate of gain is stabilized at the correct level.

Marchetti and Menaker (1950), in investigating 634 young primiparous patients, found that the average gain was 23 pounds in patients without complications, but 31 pounds in patients who developed pre-eclampsia. Since 19·1% of their cases developed pre-eclampsia, the authors concluded that young people did not realize the importance of rest and diet.

Obesity.

All women of average height who weigh over nine stone seven pounds (133 pounds) at the commencement of pregnancy are deemed to be overweight. Such excess weight is either the result of previous dietary indiscretion or of endocrine imbalance. Women of the latter group are particularly prone to pre-eclampsia, whereas the women of the former group will be found wanting in the physiological test of pregnancy on their general metabolism.

Of the women admitted with a diagnosis of pre-eclampsia to the Women's Hospital, Crown Street, Sydney, in the twelve months previously mentioned, 90·4% were either overweight to start with or had gained more than four pounds per month for a minimum period of six weeks.

An effort is made to reduce the weight of women who are overweight in the early months of their pregnancies. This serves the purpose of dietary discipline and of relieving the overloaded bodily metabolism. In the case of the very obese, every effort is made to reduce the weight throughout pregnancy. Thyroid is tolerated readily in pregnancy, and unless there is a special contraindication, proves of help in reducing the weight of these patients.

The role of the thyroid gland in pregnancy is not yet fully understood, but it is recognized that amongst its other functions it plays an important part in the treatment of some cases of sterility and the prevention of repeated abortion.

It will thus become evident that the diet advocated to control weight must be rich in protein and of sufficient quantity to control the weight gain of the patient.

Rest.

Bed rest varying from one hour a day to total bed rest is ordered according to the severity of the signs. All patients admitted to hospital are given complete bed rest. The hæmodynamics of pregnancy are probably involved in the sometimes miraculous improvement which follows complete rest in bed.

Prevention and Treatment of Anæmia.

All patients have a hæmoglobin estimation made early in pregnancy. This is repeated from time to time if clinically indicated.

The provision of an adequate diet along the lines already discussed may be the only treatment necessary to prevent or cure the common types of anæmia occurring in pregnancy. It is, however, a wise precaution to give extra ferrous iron in the second half of pregnancy (Toland, 1936; Smallwood, 1936; Corrigan[9] and Strauss, 1936; Hamilton and Wright, 1942).

Patients with a hæmoglobin value below 10 grammes *per centum* are admitted to hospital for full hæmatological investigation and appropriate treatment. Pre-eclampsia and many other complications of pregnancy and labour are commonly found in the presence of anæmia.

Reports of Cases.

The following cases illustrate the results obtained when the regime outlined is adhered to in every detail.

Mrs. K.N.W., aged thirty-four years, had had her first pregnancy terminated at thirty-three weeks by Cæsarean section because of severe preeclampsia after medical and surgical inductions had failed. She was delivered of a female baby, weighing four pounds at birth, who survived. In the second pregnancy a trace of albumin was present in the last three weeks. Spontaneous labour took place at full term and a female baby weighing seven pounds six ounces was born *per vaginam*. The baby survived. Medio-lateral episiotomy and forceps delivery were necessary because there had been a previous Cæsarean section. Only this second pregnancy was conducted under the *régime* advocated.

Mrs. M.D.S., aged forty-two years, had had a completely normal first pregnancy. In her second pregnancy some albuminuria and œdema were present in the last six weeks. In her third pregnancy she was preeclamptic in the last eight weeks. Surgical induction of labour was undertaken at thirty-eight weeks. Her fourth pregnancy was normal throughout.

This last pregnancy was the only one in which a protein-rich diet and strict weight control were employed.

In addition to the cases at the Women's Hospital, Crown Street, Sydney, I am able to report 1600 consecutive cases which I have supervised. There were no cases of eclampsia and only 17 cases of pre-eclampsia of sufficient severity to warrant the patient's admission to hospital for treatment.

Summary.

Reference has been made to some of the research into the cause of pre-eclampsia and eclampsia.

Figures for eclampsia and pre-eclampsia at the Women's Hospital, Crown Street, Sydney, have been given.

The salient features of diagnosis and treatment have been given.

The diet in pregnancy has been discussed in detail and high protein values have been advocated, with sufficient Calories to control the weight gain.

My own results have been given.

Conclusion.

The claim is made that eclampsia is preventible and that the incidence and severity of pre-eclampsia may be lessened.

Acknowledgements.

I wish to thank Sister J. B. Busby and Sister F. Kennedy for their help in compiling out-patient statistics. I also wish to thank Sister R. Wood and Miss K. E. Woolley for their help in preparing in-patient statistics.

References.

Bastiaanse, M. A. Van Bouwdijk, and Mastboom, J. L. (1949), "Prophylaxis and Treatment of Eclampsia at the University of Amsterdam Women's Clinic", *Nederlandschtijdschrift voor geneeskunde*, Volume XCIII, page 2609; quoted by J. P. Greenhill in "The 1950 Year Book of Obstetrics and Gynecology", page 119.

Best, C. H., and Taylor, N. B. (1945), "The Physiological Basis of Medical Practice", Fourth Edition, Chapter 8, page 58.

Bull, G. M., Bywaters, E. G. L., and Joekes, A. M. (1950), "Modern Trends in Obstetrics and Gynæcology", Kenneth Bowes; Chapter 19: "Management and Treatment of Extreme Oliguria and Anuria", page 301.

Burt, C. C. (1950), "The Peripheral Circulation in Pregnancy", *Edinburgh Medical Journal*, Volume LVII, page 18.

Commonwealth of Australia, National Health and Medical Research Council (1948), "Composition of Australian Foods", Special Report Series Number 4, page 56.

Corrigan, J. C., and Strauss, M. B. (1936), "The Prevention of Hypochromic Anæmia in Pregnancy", *The Journal of the American Medical Association*, Volume CVI, page 1088.

Hamilton, H. A., and Wright, H. P. (1942), "Development of Hypochromic Anæmia during Pregnancy: Response to Iron Therapy", *The Lancet*, Volume II, page 189.

Hamilton, H. F. H. (1949), "The Cardiac Output in Normal Pregnancy", *The Journal of Obstetrics and Gynæcology of the British Empire*, Volume LVI, page 548.

Keller, R. J. (1950), "Hæmodynamics in Pregnancy", *Edinburgh Medical Journal*, Volume LVII, page 33.

Marchetti, A. A., and Menaker, J. S. (1950), "Pregnancy and the Adolescent", *American Journal of Obstetrics and Gynecology*, Volume LIX, page 1013.

Mayes, B. T. (1950), "A Textbook of Obstetrics", Chapter XIX, page 414.

Mukherjee, C. L., and Govan, A. D. T. (1950), "Blood Pressure and Prognosis in Toxæmia of Pregnancy", *The Journal of Obstetrics and Gynæcology of the British Empire*, Volume LVII, page 946.

McCance, R. A., Widdowson, E. M., and Lehman, H. (1942), "Effect of Protein Intake on Absorption of Calcium and Magnesium", *Biochemical Journal*, Volume XXXVI, page 686.

Palmer, A. J., and Walker, A. H. C. (1949), "The Maternal Circulation in Normal Pregnancy", *The Journal of Obstetrics and Gynæcology of the British Empire*, Volume LVI, page 537.
Sherman, H. C. (1945), "Chemistry of Food and Nutrition", Seventh Edition.
Smallwood, W. C. (1936), "The Anæmia of Pregnancy", *British Medical Journal*, Volume II, page 573.
Toland, O. J. (1936), "Incidence and Treatment of Secondary Anæmia in Out-patient Maternity Patients", *American Journal of Obstetrics and Gynecology*, Volume XXXI, page 640.
Tompkins, W. T. (1941), "The Significance of Protein Nutrition in Health and Disease", *The Journal of the International College of Surgeons*, Volume IV, page 147.
Williams, P. F. (1945), "Importance of Adequate Protein Nutrition in Pregnancy", *The Journal of the American Medical Association*, Volume CXXVII, page 1055.

APPENDIX: DIET LISTS.

I: Normal Pregnancy Diet (Calories 2400 to 2500).

Lean Meat: At least one large serving daily.
Eggs: One daily (at least five per week).
Vegetables: Three or four vegetables daily, including yellow and leafy vegetables.
Fruit: Two or three pieces daily.
Bread: Two or three thin slices a day.
Cereals: Small helpings of rolled oats, wheatmeal or oatmeal.
Milk: One to two pints a day.
Cheese: One ounce a day.
Butter: One ounce or less.
Avoid fats and starchy foods, such as cakes, biscuits and puddings.
Avoid excessive salt.
Do not eat between meals.

II: Toxæmia Saltless Diet (Calories 2100).[1]

Breakfast.	Ozs.	Protein. Gm.	Fat. Gm.	CHO. Gm.	Na. Gm.	Thiamin. Mgm.
Eggs	1 egg	6	6	—	·070	·075
Chop	1½	9	10	—	·042	·030
Bread, s.f.[2]	1	2	—	16	·005	·029
Butter, s.f.	¼	—	6	—	—	—
Apple	3	1	—	8	·009	·039
		18	22	24	·126	·173
Dinner.						
Meat	3	18	20	—	·072	·051
Yellow vegetables, s.f.	3	2	—	9	·018	·030
Green vegetables, s.f.	3	1	—	4	·034	·060
Bread, s.f.	1	2	—	16	·005	·029
Butter, s.f.	¼	—	6	—	—	—
Stewed fruit (including sugar)	3	1	—	14	·009	·039
		24	26	43	·138	·209
Tea.						
Cold meat	2	12	14	—	·048	·034
Cheese	½	3	5	—	·130	·004
Lettuce	1	—	—	—	·006	·021
Tomato	3	—	—	4	·018	·051
Celery	1	—	—	—	·018	·009
Bread, s.f.	1	2	—	16	·005	·029
Butter, s.f.	¼	—	6	—	—	—
Orange	3	1	—	8	·009	·063
		18	25	28	·234	·211
Milk	38	36	42	50	·523	·420
	Total	96	115	145	1·021	1·013

Total protein: 96 grammes.
First-class protein: 84 grammes.
Calories: 2000 and sugar in tea *et cetera*, 2100.

III: Toxæmia Saltless Diet (Calories 1900).

No salt on plate or in cooking.
No salty foods such as bacon, ham, corned beef, salty fish, sausages, pickles, "Vegemite", peanut butter.
No bicarbonate of soda.
No antacid powders.
No foods made from fat, sugar or flour.

Foods Which Should be Taken Daily.

Milk: Two pints.
Meat: At least one large serving.
Cheese: One to two ounces.
Butter: A little.
Eggs: Two daily.
Fruit: Two or three pieces.
Vegetables: As much as desired, but only small helpings of potato, peas, sweet potato, corn, broad beans, parsnips.
Bread: Three thin slices.

IV: Toxæmia Saltless Diet (Calories 1750): Avoid Salt.

Foods Which Are to be Taken Daily.

Milk: One and a half pints.
Meat: Four ounces. This is equivalent to two large chops or two large lean slices of roast meat.
Cheese: One ounce.
Butter: A little.
Eggs: One or two daily.
Fruit: Two or three pieces.
Vegetables: Two or more types, particularlyy yellow and green leafy vegetables.
Bread: Two thin slices.

V: Reducing Diet (Calories 1100).

4 *a.m.*: Milk coffee (no sugar).
Breakfast:
One egg or one chop.
One piece of salt-free bread and butter.
One piece of fruit.
Tea with milk (no sugar).
10 *a.m.*: Six ounces of special milk.[1]
Dinner:
Lean meat.
Salt-free vegetables.
One piece of fresh fruit.
3 *p.m.*: Six ounces of special milk.
Tea:
Lean cold meat.
Lettuce, celery, tomato.
One piece of salt-free bread and butter.
One piece of fruit.
Supper: Six ounces of special milk.

[1] Figures from Sherman (1945); National Health and Medical Research Council (1948).
[2] s.f. = salt-free.

"PHENIODOL" EXCRETION: OBSERVATIONS ON THE URINE OF PATIENTS WITH HEPATIC DISEASE.

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DOHRN AND DIEDRICH in 1940 introduced α-phenyl-β(4-hydroxy-3:5-diiodophenyl) propionic acid as a radio-opaque substance suitable for X-ray examination of the gall-bladder. Since then this substance has been widely used, under the trade names of "Priodax", "Pheniodol" or "Biliselectan", and found to be a good contrast medium.

English and American radiological journals contain little reference to its pharmacology beyond referring to the fact

[1] Special milk is made from two ounces of dried skimmed milk in 18 ounces of water with suitable flavouring, and beaten to a creamy consistency. This gives all the elements of fresh milk without the fat content.
[2] Royal Prince Alfred Hospital Medical Board's Fellow in Medicine.
[3] Supported by a grant from the National Health and Medical Research Council.

that it is absorbed from the intestinal tract, excreted in the bile and reabsorbed in the intestine, and that ultimately 60% to 80% is excreted in the urine.

During the course of an unrelated investigation it was necessary to measure the amount and rate of renal excretion of "Pheniodol" in normal subjects and in patients with certain hepatic disorders. This paper records our observations, which essentially confirm and extend the work of R. Crismer of Liège. He reported his findings in dogs and man in 1947, but they do not appear to have reached the notice of most English and American workers.

Methods.

Concentration of α-phenyl-β(4-hydroxy-3:5-diiodo-Phenyl) Propionic Acid in Urine.

To five millilitres of urine 0·5 millilitre of 50% sulphuric acid is added, and extraction is carried out twice with 10 millilitres of ether. The ether is evaporated and the iodine in the residue is determined according to the method of Canbäck. Standards were prepared from pure α-phenyl-β(4-hydroxy-3:5-diiodophenyl) propionic acid (a gift from Boots Pure Drug Company (Australia) Proprietary, Limited).

Administration to Controls and Patients.

Oral doses of "Pheniodol" were administered to fasting controls and to experimental subjects and were followed by a draught of water. The dose given to the controls varied between 1·75 and 3·0 grammes and that to the patients between 2·0 and 2·5 grammes (a range of 24 to 42 milligrammes per kilogram for all subjects). Copious fluids were taken for the next few hours and all urine was saved. Urine specimens were collected every hour or every two hours for eight to twelve hours, and subsequent urine specimens were arranged into twelve-hour periods to cover a total collecting period of seventy-two to eighty hours. Meals were allowed after the eighth hour. X-ray examination of the gall-bladder was made after eight to twelve hours. None of the subjects vomited after taking the test doses. Diarrhœa was observed in only one subject (a control), but this was mild and transient.

The patients studied were as follows.

CASE I.—The subject was a man (Ho) suffering from cirrhosis of the liver. He was aged forty-nine years, and his alcohol intake had been excessive for many years. He had a past history of ascites and hæmatemesis, but was not jaundiced. The serum bilirubin content was 0·2 milligramme per 100 millilitres, the serum thymol turbidity test produced a strongly positive result, the serum alkaline phosphatase content was 9·6 King-Armstrong units, and the total serum protein content was 5·1 grammes per 100 millilitres. Needle biopsy of his liver revealed active portal cirrhosis.

CASE II.—The subject was a woman (Mg) suffering from active hepatitis progressing to portal cirrhosis. She was aged twenty-six years and was unmarried, and had had a clinical attack of infectious hepatitis in January, 1949. Jaundice persisted till her admission to the unit in October, 1950, but she had not experienced ascites nor had a hæmatemesis. Her liver was impalpable, but her spleen was moderately enlarged. There was no clinical evidence of ascites. Her serum bilirubin concentration was 4·25 milligrammes per 100 millilitres, the serum thymol turbidity test produced a positive result, serum alkaline phosphatase content was 27 King-Armstrong units, and the total serum protein content was 7·6 grammes per 100 millilitres. Needle biopsy of her liver revealed active hepatitis progressing to portal cirrhosis.

CASE III.—The patient was a married man (L) suffering from biliary obstruction, the result of adenocarcinoma of the ampulla of Vater. He was aged fifty-nine years, was deeply jaundiced, and had bile in his urine and clay-coloured stools. Prior to operation the serum bilirubin content was 31 milligrammes per 100 millilitres, the serum alkaline phosphatase content was 50 King-Armstrong units, the serum thymol turbidity test produced a negative result and the total serum protein content was 8·1 grammes per 100 millilitres. Needle biopsy of the liver revealed early biliary cirrhosis. Operation revealed adenocarcinoma of the ampulla of Vater, and a cholecystjejunostomy was performed with subsidence of his jaundice and general symptomatic relief.

"L(i)" refers to this patient prior to operation, "L(ii)" after operation.

Results.

The amount of "Pheniodol" found in the urine specimens is expressed as a percentage of the administered dose for each subject. The excretion curves for the controls receiving widely different doses were practically identical when plotted in this manner. This method has been employed to eliminate variations due to differences in body size.

Tables I and II contain the results of studies on two controls and three patients.

It is apparent in Table I that three patients suffering from hepatic disease excreted less "Pheniodol" in their urine in three days than did the controls. But "L" excreted more than the controls after biliary drainage had been established (L(ii)).

Table I also shows that the three patients suffering from hepatic disease excreted more than the controls during the first twelve hours, a little less in the second twelve hours, and very much less during the second and third days. The diminished excretion in the last forty-eight hours accounted for the diminished total excretion.

TABLE I.
Excretion of "Pheniodol" in the Urine after Oral Dosage.

Subject.	Dose. (Milligrammes per Kilogram.)	Percentage of the Dose Excreted.				
		Total in 72 Hours.	0 to 12 Hours.	12 to 24 Hours.	24 to 48 Hours.	48 to 72 Hours.
Controls	24 to 40	69 (64–73)	30·0	17·8	15·9	4·9
"Ho" ..	42·4	60	36·5	15·5	6·6	1·2
"Mg" ..	35·1	59	34·6	15·8	6·7	1·6
"L(i)" ..	42·0	47	33·6	9·8	3·2	1·0
"L(ii)" ..	40·3	78	36·5	25·4	13·9	3·0

The increased excretion during the first few hours is made more striking when the excretion rates are expressed as percentages of the total amount excreted in the urine in three days for each individual—that is, expressed in a manner to show how each individual dealt with the amount of "Pheniodol" he was ultimately to excrete in the urine. It was found that the controls excreted 18% between the fourth and eighth hours, but "Mg" and "Ho" excreted 28% and "L(i)" 35% in the same period of time.

The excretion rates of the controls and patients reached their maxima at approximately the same time, the sixth hour after the dose was taken. The maximal excretion rates in the patients (1·74 to 2·87 milligrammes per minute) were somewhat greater than in the controls (1·02 to 1·86 milligrammes per minute), and this difference was more pronounced when referred to dosage (Table II).

TABLE II.
Maximum Excretion Rates of "Pheniodol" in the Urine after Oral Administration.

Subject.	Time After Oral Administration in Hours.	Maximum Rate.	
		Milligrammes per Minute.	Percentage of Dose per Minute.
Controls	4 to 7	1·02 to 1·86	0·051 to 0·064
"Ho"	6 to 8	1·74	0·070
"Mg"	4 to 6	1·85	0·093
"L(i)"	6 to 7	2·87	0·094
"L(ii)"	7 to 10	1·92	0·077

Though the observations are limited, the decrease in excretion rates appeared to follow a standard logarithmic pattern after the first twelve hours in all subjects. It was found that the hourly excretion rate fell by 50% every sixteen hours in the controls, every seven hours in "L(i)" and "Ho", and every 9·5 hours in "Mg". Thus the excretion rates of the three patients suffering from hepatic disease decreased about twice as fast as those of the controls. After operation the excretion rate in "L(ii)" fell 50% every 10·5 hours.

It is to be noted that comparison of the results in "L" with biliary obstruction and after the reestablishment of intestinal biliary drainage showed a considerable change towards normal. His total excretion became greater than that of the controls, but this was owing to a greater excretion in the first twenty-four hours, as the excretion in the second and third days was still diminished.

Discussion.

The absorption and excretion of "Pheniodol" may be represented diagrammatically as in Figure I.

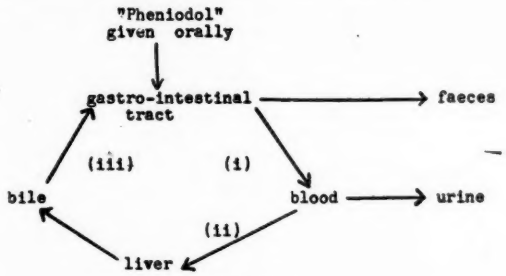

FIGURE I.

Crismer found that 60% to 80% of the ingested dose was excreted in the urine during the first three days, both in man and in the dog, and that the remainder was excreted in the fæces. The renal excretion amounted to 50% of the dose in the first twenty-four hours and a similar amount was recovered from bile fistulæ in dogs. Crismer also observed, in dogs, that the presence of bile salts greatly facilitated the absorption from the intestinal tract. He reported that 50% of the "Pheniodol" injected intravenously was excreted into the bile and could be recovered from a fistula.

It is reasonable to assume that the amount of "Pheniodol" excreted in the urine depends primarily on the concentration in the blood-stream. One may then say that the urine excretion will depend on the following: (i) the amount and rate of absorption; (ii) the amount and rate of hepatic extraction; (iii) the amount and rate of biliary excretion; (iv) the amount and rate of reabsorption; (v) the ability of the kidney to excrete "Pheniodol".

The data presented in this report may be interpreted as indicating that the patients had the following:

1. A diminished intestinal absorption of "Pheniodol". A smaller proportion of the ingested dose was excreted by the patients than by the controls ((i) in the diagram).

2. A diminished hepatic extraction of "Pheniodol" from the blood-stream. In spite of a decreased total excretion, the early excretion was greater than in the controls. A diminished hepatic extraction could result is a relatively high blood concentration in spite of a somewhat reduced total absorption ((ii) in the diagram). A higher blood concentration would result in an increased renal excretion. The maximal excretion rates in the patients were no lower than in the controls—they tended to be higher, but occurred at approximately the same time after the dose was taken. These high excretion rates were not related to dosage, for they were even higher than those of the controls if calculated as percentages of the administered dose. It is difficult to envisage any cause for these high rates except as a result of greater blood concentrations. Crismer's finding that intravenously injected "Pheniodol" appears in the bile disposes of any argument that hepatic extraction requires an initial presentation in the portal blood.

3. A diminished biliary excretion of "Pheniodol" and subsequent reabsorption from the intestine. The total amount excreted was less than in the controls. The rapid decrease in excretion rates reflected the virtual absence of "hepato-enteric" circulation of "Pheniodol" ((iii) in the diagram). Little that was excreted into the intestine in the bile would be reabsorbed. Not only did the patient "L", after establishment of biliary drainage, excrete more in seventy-two hours, but the slower decline in excretion rate indicated some biliary excretion and intestinal reabsorption.

4. At least a normal capacity to excrete "Pheniodol" in the urine in the dosage used. The maximal amounts excreted in the urine per minute exceeded those found in the controls. None of the patients had evidence of impaired renal function.

This interpretation is supported by X-ray studies. Clear-cut shadows of the controls' gall-bladders were obtained eight to ten hours after "Pheniodol" had been taken, but it was not so with the patients. One patient in particular, "Mg", had no gall-bladder shadow, but much of the "Pheniodol" was in the bowel—the opposite of the controls.

Crismer's finding that bile salts facilitated the absorption of "Pheniodol" might suggest the clinical use of bile salts to assist in the performance of "Graham's test" on the jaundiced patient. Our observations would not support such a contention. There was a high maximum excretion rate in all three patients, though only two of them, "L(i)" and "Mg", had raised serum bilirubin levels indicative of biliary obstruction. Whilst the role of bile salts may be of importance, it would appear that failure of the liver to extract "Pheniodol" from the blood-stream is more important in the failure to outline the gall-bladder in the performance of Graham's test on patients with liver disease.

Summary.

Observations have been made on the excretion of α-phenyl-β(4-hydroxy-2:5-diiodophenyl) propionic acid ("Pheniodol") in the urine of normal subjects and in that of patients with hepatic disease following standard oral dosage.

A diminished total excretion of α-phenyl-β(4-hydroxy-3:5-diiodophenyl) propionic acid was found in the patients' urine, but in the first twelve hours more was excreted by the patients than by the controls.

The results are interpreted to indicate that these patients had both a diminished absorption and a diminished hepatic extraction of α-phenyl-β(4-hydroxy-3:5-diiodophenyl) propionic acid, the latter appearing to be the more important factor.

References.

Crismer, R. (1947), *"Recherches nouvelles sur la pharmacodynamie du bilisélectan: son absorption intestinale, son excrétion biliaire et urinaire, son comportement dans la vésicle biliaire", Journal de radiologie et d'électrologie,* Volume XXVIII, page 229.

Crismer, R., and Brull, L. (1946*a*), *"Vitesse et mode d'élimination de l'acide (oxy-4-diiodo-3,5-phényl)-β-phényl-α-propionique chez l'homme", Comptes rendus des séances de la Société de biologie et de ses filiales,* Volume CXL, page 907.

——— (1946*b*), *"Excrétion biliaire, urinaire et intestinale de l'acide - β - (oxy - 4 - diiodo,5 - phényl) - α - phényl - propionique", Comptes rendus des séances de la Société de biologie et ses filiales,* Volume CXL, page 1042.

Canbäck, T. (1944), *"Bestämning av jod i tetrajodftaleinnatrium", Särtryck ur Svensk Farmaceutisk Tidskrift,* Volume XXVIII, page 381.

Canbäck, T., and Wallenburg, B. (1945), "The Determination of Iodine in Thyroid and in its Preparation", *Särtryck ur Svensk Farmaceutisk Tidskrift,* Volume XLIX, page 861.

THE VALUE AND LIMITATIONS OF X-RAY EXAMINATION IN ASSESSING DISEASE OF THE GALL-BLADDER.[1]

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FOLLOWING on Abel and Rowntree's work, in which they showed that the phenolphthaleins as a class were largely excreted in the bile, Graham and Cole in 1924 first demonstrated that an opaque shadow was produced in the gall-bladder after intravenous injection of phenolphthalein containing iodine. Thus was born the first cholecystogram. Similar preparations were used from then onwards until 1940 when "Pheniodol" was introduced and this is now almost universally used.

[1] Read at a meeting of the College of Radiologists (Australia and New Zealand) on September 28, 1951, at Sydney.

Pharmacology of "Pheniodol".

The new radioopaque compound α-phenyl-β(4-hydroxy-3:5-diiodophenyl) propionic acid was discovered by Dohrn and Diedrich in 1940, and was first prepared in Germany and France under the name of "Biliselectan", then in England under the name of "Pheniodol", in the United States of America as "Priodax" or "Dikol", and in Belgium as "Bilopsyl".

Although Junkmann had shown that in the rabbit 50% of the material is eliminated in the urine in twenty-four hours, and in man 33·4% to 53·7% in twenty-four hours, most of the pharmacology of this drug was worked out in France by Crismer in 1947. The following is a summary of his findings. My attention was drawn to this work by Dr. C. R. B. Blackburn, who independently obtained similar findings which are reported elsewhere in this issue, and which were made before he was aware of the French studies.

Intestinal Absorption of "Biliselectan".

In fasting dogs maximum blood levels of "Biliselectan" occur at eight to nine hours; during a meal the maximum is reached in three to four hours; absorption is then more rapid if the drug is taken in the course of a meal. If the common bile duct is tied absorption is maximal at eight to ten hours, but if bile salts are administered with the duct tied absorption is again maximal in three to four hours. It would then appear advisable for "Pheniodol" to be taken during or at the end of a meal for rapid absorption, which is assisted by the presence of bile salts.

Excretion.

The drug is excreted by the liver into the biliary channels and thence into the intestine, where it is mostly reabsorbed into the portal circulation, being excreted mainly by the kidneys. Crismer showed that in man after five days 61% to 81% was eliminated via the urine and 7% to 33% via the fæces. The urinary excretion lessens the risk of using this material in hepatic disease. The use of tetraiodide was risky in liver disease, as urinary excretion of this material is insignificant. In the absence of severe renal disease, then, there would appear to be no risk in repeating the Graham's test in one to three days or in giving a double dose.

Absorption by the Gall-Bladder Mucosa.

Studies in the dog by the injection of "Pheniodol" into the gall-bladder after ligation of the cystic duct have shown that 58% of the material is absorbed in six hours. When formalin cholycystitis is produced experimentally in a dog, the quantity of "Biliselectan" absorbed rises to 83·6% in six hours. The inflamed gall-bladder under experimental conditions is then more permeable to "Pheniodol" than the normal gall-bladder mucosa. This, then, may be one of the factors explaining the poor opacity or non-opacity of the gall-bladder when cholycystitis is present and in the absence of cystic duct obstruction.

Summary.

1. After a meal "Pheniodol" reaches a maximum concentration in the blood-stream in three to four hours.
2. Its absorption is greatly assisted by the presence of bile salts.
3. It is excreted by the liver in the bile.
4. Most of the "Pheniodol" which is excreted in the bile is reabsorbed, the fæcal elimination playing only an accessory part in the elimination of the dye, which is principally excreted in the urine. Complete elimination of "Pheniodol" generally occurs in five days.
5. "Pheniodol" is partially absorbed by the mucosa of the gall-bladder, but this is slow. This absorption is increased in acute experimental cholecystitis.

Physiology of the Gall-Bladder and Bile Duct System.

The gall-bladder holds approximately 50 millilitres of fluid. Its function is that of concentration of bile by absorption of water and electrolytes. It effects roughly a tenfold concentration for water and salts, but can concentrate bilirubin twenty times.

Bile flows into the gall-bladder via the cystic duct, provided the sphincter of Oddi is closed. The tone of this sphincter is increased during fasting and if alkali is present in the stomach. A certain head of pressure is required before bile enters the gall-bladder. As concentration proceeds in the gall-bladder, more bile will flow into it. The liver produces about 500 to 1500 millilitres of bile in twenty-four hours, and this concentrated ten times would fill the gall-bladder one to three times, so that the gall-bladder can hold all the bile excreted by the liver. Once "Pheniodol" has been swallowed, then no further food should be taken until the gall-bladder concentration has occurred and films have been taken. It may be worth while to give alkalis by mouth to increase the tone of the sphincter of Oddi.

The ability of the gall-bladder to concentrate "Pheniodol" efficiently depends upon the following factors: (i) adequate absorption (already dealt with); (ii) a normally functioning liver; (iii)) a patent cystic duct; (iv) a closed sphincter of Oddi and good tonus in the biliary system; (v) a normally functioning gall-bladder. In the interpretation of cholecystograms all these factors must be taken into account.

Fats cause a greater acceleration of flow of bile from the liver than any other food—the yolk of hen's eggs is especially effective. There is relaxation of the sphincter mechanism and bile flows into the intestine. The gall-bladder empties by dilution, and actual contractions can be seen, although there is not much muscular tissue in its structure. There is believed to be a reciprocal innervation between the gall-bladder and the sphincter of Oddi mechanism.

The ability of the gall-bladder to empty itself when fats enter the duodenum depends upon the following factors: (i) patency of the cystic duct and the common bile duct; (ii) relaxation of the sphincter mechanism. Dyskinesia of the gall-bladder and sphincter of Oddi mechanism is a common cause of misdiagnosis of gall-bladder disease.

Factors in the Interpretation of the Graham's Test Result.

Anatomical and Functional Physiological Variations of the Normal Gall-bladder.

Mills in 1917 adequately stressed the relationship of anatomical habitus to visceral form and function. This has an important bearing on the position and function of the gall-bladder and therefore on the interpretation of the Graham's test result. The heavy hypersthenic individual has a gall-bladder in a high position lying horizontally producing a circular or oval shadow, and the asthenic subject has a long, narrow organ in a low position. It is reasonable to expect the hypersthenic to have a gall-bladder with a good tonus and greater activity than the asthenic. Curiously, the asthenic type is less likely to suffer from gall-bladder disease.

Congenital conditions such as convoluted cystic duct, abnormal cystic artery or septa such as the Phrygian cap may cause disturbances in the filling and emptying mechanism of the gall-bladder. However, these variations, as well as external adhesions such as those from chronic duodenal ulceration, may often be associated with gall-bladder disease.

Gas Shadows Obscuring the Gall-bladder.

One of the chief difficulties in interpretation is when the gall-bladder shadow is overshadowed by that of other structures such as the colon and the spinal column. Radiologists take their films mainly with the subject in the prone position. The Mayo Clinic favours the postero-anterior view with the patient lying on his right side, which permits the gall-bladder to gravitate somewhat away from the bowel and gives a better view of the bile ducts.

Non-filling or Poor Filling of the Gall-bladder.

One must first be sure that the "Pheniodol" has been absorbed satisfactorily and that liver function is adequate.

Only acute or advanced chronic liver disease will interfere with the test significantly. Renal disease such as chronic nephritis will not. With regard to other diseases, Good and Kirklin investigated 733 cases of peptic ulcer, pernicious anæmia, thyrotoxicosis, myxœdema, diabetes, obesity, pulmonary tuberculosis and chronic appendicitis, and found 167 instances of poor or absent gall-bladder shadows on X-ray examination; of these, 104 gall-bladders were examined at operation or autopsy, the gall-bladder disease was confirmed and only two gall-bladders were normal. This would indicate that extensive diseases, both metabolic and abdominal, have nothing to do with the ability of the gall-bladder to concentrate or excrete the contrast mediums.

Controversy still exists as to the worth of cholecystography in the presence of jaundice. Feldman maintains that cholecystography is not contraindicated in jaundice, and that the test may be of considerable assistance in the differential diagnosis of hepatocellular and obstructive jaundice. However, our own experience at Royal Prince Alfred Hospital is quite the reverse.

Another cause of non-filling may be physiological stasis, which can result if little or no fat has been eaten for two to three days prior to the test. Thick, concentrated bile will be present in the gall-bladder, and the "Pheniodol" may not enter in sufficient concentration. It would seem rational to give a meal containing fat prior to administration of "Pheniodol" (Brewer).

If the technique has been correct and there is no filling, then (i) the medium has not reached the gall-bladder because of obstruction in the cystic duct, or (ii) it has reached the gall-bladder but the mucosa is so extensively damaged that it cannot concentrate it, or (iii) it has been absorbed too quickly through the gall-bladder wall. In all cases of non-filling the test should be repeated one to five days later. If the patient is obese or heavily built, consideration should be given to the double-dose technique.

Intensity of the Shadow.

As the intensity of the shadow cannot be measured scientifically but remains merely a personal opinion, there will always be difficulty in interpretation. Some radiologists compare the density with that of the ribs. Minor degrees of defect should be ignored. Mayo Clinic workers reported that in their experience 95% of poorly filling gall-bladders were diseased. On the other hand, a diseased gall-bladder (for example, strawberry gall-bladder) may give a shadow of normal intensity. In all cases of poor filling the test should be repeated, preferably with the use of a double dose of "Pheniodol".

Rate of Emptying of Gall-bladder.

It is often maintained by radiologists that after a fatty meal the gall-bladder shadow should show the organ to be partially empty in one hour and completely so in three to six hours. Failure of the shadow to disappear may indicate a failure of the gall-bladder and bile duct mechanism to relax or some mechanical obstruction in the gall-bladder, cystic or common bile duct or such conditions as abnormal cystic artery or convoluted cystic duct. Biliary dyskinesia is accepted as being a true entity, and spasm of the sphincter of Oddi can be produced in some subjects when they are given morphine.

Slow emptying does not necessarily mean gall-bladder disease. Failure of the gall-bladder to contract may be due to gall-bladder disease, but it is not in itself conclusive evidence. Dann and Koritschoner, in a clinical and cholecystographic study of the motor activity of the gall-bladder in out-patients with no past or present history of abdominal complaints, found a wide range of normal emptying rate within the first twenty-four hours, in one case the gall-bladder taking forty-eight hours to empty.

On physiological grounds it is difficult to see how delayed emptying alone can be attributed to chronic gall-bladder disease in the absence of obstruction; yet radiologists frequently incriminate the gall-bladder on these grounds.

Gall-stones.

It is estimated that 10% of gall-stones are radioopaque. Therefore a plain X-ray examination of the abdomen should precede the Graham's test. By cholecystography approximately 50% of stones can be visualized. The identification of gall-stones is always indicative of gall-bladder disease. Radiologists may increase their score of stones by using the fatty meal technique to demonstrate stones in the fundus of the contracted gall-bladder.

Discussion.

When any disease process is suspected and the radiologist is asked to help, a careful analysis of symptoms and signs must be considered side by side with the radiological findings before a rational opinion can be given. In biliary tract diseases this careful evaluation is of the greatest importance. When the history and physical findings of gall-bladder disease are clear-cut there is scarcely any need for cholecystography; when gall-stones can be demonstrated by the radiologist the interpretation is also straightforward. It is when the clinician is in doubt that clinical and radiological evidence must be carefully considered together and a reasonable deduction made on all the evidence. A normal cholecystogram does not rule out disease of the gall-bladder. In 5% to 10% of cases a normal cholecystogram is found when distinct gall-bladder disease is present. Further, some 30% to 40% of gall-stones will not be revealed by radiology.

When the test has been carefully carried out with due regard for the pharmacology of the drug, and when liver function is known to be adequate, the accuracy of the test is of a high order. When there is doubt in the interpretation of the result of this test it should always be repeated. The final judgement as to the presence of gall-bladder disease should always rest with the clinician.

References.

Abel, J. J., and Rowntree, L. G. (1909), "On the Pharmacological Action of Some Phthaleins and their Derivatives, with Especial Reference to their Behaviour as Purgatives", *The Journal of Pharmacology and Experimental Therapeutics*, Volume I, page 231.

Brewer, A. A. (1947), "Physiological Stasis: A Cause of Cholecystographic Error", *American Journal of Roentgenology*, Volume LVIII, page 110.

Crismer, R. (1947), *"Recherches nouvelles sur la pharmacodynamie du bilisélectan: son absorption intestinale, son excrétion biliaire et urinaire, son comportement dans la vésicle biliaire", Journal de radiologie et d'électrologie*, Volume XXVIII, page 229.

Dann, D., and Koritschoner, R. (1946), "A Clinical Study of Normal and Pathologic Motor Activity of the Gall-bladder", *Radiology*, Volume XLVII, page 494.

Dohrn, M., and Diedrich, P. (1940), *Deutsche medizinische Wochenschrift*, Volume LXVI, page 1133.

Feldman, M. (1941), "A Review of the Present Status of Cholecystography in the Radiological Diagnosis of Gall-bladder Disease", *The Review of Gastroenterology*, Volume VIII, page 320.

Graham, E. A., and Cole, W. H. (1924), "Roentgenologic Examination of the Gallbladder, Preliminary Report of a New Method Utilizing the Intravenous Injection of Tetrabromphenolphthalein", *The Journal of the American Medical Association*, Volume LXXXII, page 613.

Kirklin, B. R. (1948), "New Position for Cholecystography", *American Journal of Roentgenology and Radium Therapy*, Volume LX, page 263.

Mills, R. W. (1917), "Relation of Bodily Habitus to Visceral Form, Position, Tonus, and Mobility", *American Journal of Roentgenology and Radium Therapy*, Volume IV, page 155.

THE VALUE AND LIMITATIONS OF X-RAY EXAMINATION IN ASSESSING DISEASE OF THE GALL-BLADDER.[1]

By Kenneth W. Starr.

The surgery of the biliary system is so complex, and fraught with so many difficulties, mechanical, physiological and pathological, that he would be foolish indeed who undertook the surgical management of biliary disease without a complete assessment of his patient. This ultimate assessment is now and always will be clinical. There is no substitute for this evaluation; but many factors contribute to a correct appraisal. Not the least of these is

[1] Read at a meeting of the College of Radiologists (Australian and New Zealand) on September 28, 1951, at Sydney.

the radiological examination of the biliary system. As the dye is excreted in the bile, disturbances may be encountered at any stage between its secretion by the liver parenchyma and its entry into the duodenum. Failure of excretion of the dye may therefore be related to disturbed liver function as much as to mechanical obstruction of the biliary tree.

I cannot stress too strongly my firm conviction that only the clinical features can differentiate the various causes of these conditions.

From the surgeon's viewpoint there are two main groups of cases: (i) those in which gall-stones are present, (ii) those in which no gall-stones are demonstrable.

When Gall-stones are Present.

The presence of symptoms (especially those due to impaction or transit of a stone), the fear of obstruction of the common bile duct and the dread of cancer of the gall-bladder present strong arguments for operation. The greatest assistance may be derived from a plain X-ray film of the upper part of the abdomen in some cases when a mass of stones can be demonstrated in the common bile duct. In such cases the clinical features may closely mimic an obstructing pancreatic carcinoma. Stones, too, may be demonstrated in the gall-bladder if they are heavily calcified.

However, it is more common to find that the stones are revealed as filling defects during Graham's test. Another occasion for a plain X-ray examination with a contrast medium presents when, after the common bile duct has been drained, cholangiography is performed to determine whether residual stones have been overlooked at operation.

When No Gall-stones are Demonstrable.

Cases in which no gall-stones are demonstrable may be further subdivided into three groups, as follows.

1. The Liver Fails to Excrete the Dye.

The therapeutic problem in cases in which the liver fails to excrete the dye is one of the most difficult in surgery, and it not seldom happens that cholecystectomy is performed without relief of symptoms because the only indication for the operation is a non-filling gall-bladder found in Graham's test. It is important to determine whether the liver is capable of excreting the dye, for in jaundice and hepatitis hepatic dysfunction may vitiate the radiological test. This is true not only in obvious jaundice, but also in subclinical jaundice, of which the only manifestations may be a trace of urinary bile and a raised blood bilirubin content. The enlarged tender liver of hepatitis should not escape most clinicians. Obstruction of the common bile duct by stone, neoplasm or hydatid cyst will also present similar X-ray findings owing to the associated jaundice.

2. The Gall-bladder Fails to Concentrate the Dye.

The history indicates the degree of severity of the symptoms. Flatulent dyspepsia alone is rarely considered worthy of surgical intervention, because the associated liver dysfunction may be the real cause of the symptoms which do not abate after removal of the gall-bladder. He would be a hardy surgeon indeed who would remove the gall-bladder purely on the radiological report. The situation is far different, however, when gall-bladder colic occurs, for biliary mud or frank stones may be present without being demonstrated by the radiograph. Poor filling of the gall-bladder may also be encountered when the features are those of subacute or chronic pancreatitis. In such cases mere cholecystectomy fails to relieve the symptoms of pancreatic dysfunction. The dyspepsia and fatty diarrhœa are often combined with a high blood amylase level in such cases.

An interesting series of events has twice come to my notice and made possible an accurate appraisal of the symptoms. An elderly female patient, known to have had a large gall-stone for years, presents with clinical and radiological findings of a duodenal ulcer. This indicates that the stone (not now visible) is ulcerating through a fistulous opening into the duodenum. In these cases the X-ray findings are of the greatest value if intestinal obstruction is to be avoided.

3. The Dye Concentrates Well.

Despite perfect concentration, a pathological state causing symptoms may obtain in the gall-bladder. In the Phrygian cap loculation of the viscus, gall-bladder colic often occurs and necessitates cholecystectomy. A similar series of symptoms may accompany a papilloma or frank carcinoma in the infundibulum.

Conclusion.

Finally, let me again emphasize my point that a diseased gall-bladder according to Graham's test is but one feature in a complex of symptoms and signs which require accurate evaluation before treatment is undertaken.

JAMES LAIDLAW MAXWELL: A GREAT MEDICAL MISSIONARY STATESMAN.

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THE China of the last century and a half presented a wonderful opportunity for enterprise and achievement to the medical missionaries who lived and worked there. With no understanding of science or knowledge of anatomy or surgery, a medicine based on tradition, no corporate medical profession and no conception of hospitals or nursing, but only a cast-iron anti-foreign conservatism and self-sufficiency, the situation was indeed a challenging one.

Of all those who contributed to the building of modern medicine in that land there is no one, Chinese or foreign, who has made such an outstanding and significant impact on the profession as Dr. James Laidlaw Maxwell, who died of cerebral malaria at Hangchow, just south of Shanghai, on August 10, 1951. Obituary notices have appeared in *The Times* and the *British Medical Journal*; but neither of these does justice to the stature of this man, and there are features of his life and work which give it an interest in the Pacific far beyond the confines of China.

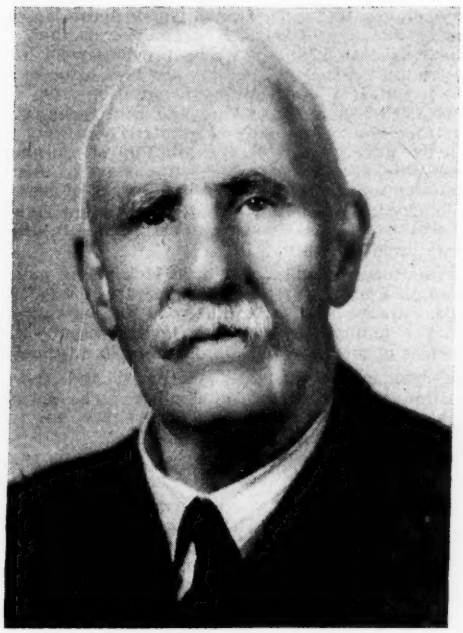
He was born in 1873, eight years after his father, James Maxwell, had begun service as a medical missionary under the English Presbyterian Mission at Tainan, Formosa. In 1901 he succeeded to the superintendency of his father's old hospital, which, with an interlude as major in the Royal Army Medical Corps from 1915 to 1919, he carried on until 1923.

It was here that his distinguished qualities first became evident. Holding the degree of doctor of medicine of the University of London, he soon acquired a wide knowledge of the incidence and distribution of disease on the Chinese mainland, amplified by various journeys inland even as far as Thibet. In 1910, in cooperation with Dr. W. H. Jefferys, he published "The Diseases of China", and in 1929 he himself brought out a second edition, which still remains the standard work on the subject. As a surgeon, too, he was a man of enterprise and strong initiative, as his various contributions to *The Chinese Medical Journal* bear evidence.

But it was leprosy to which he particularly devoted himself, doing pioneer work, which has not yet been revised, in mapping out its incidence throughout the country. He soon became known as its leading exponent in China, from 1927 to 1940 holding the position of medical adviser to the International Mission to Lepers and to the Chinese Mission to Lepers. He was associate editor of the *International Journal of Leprosy* from 1931 to 1948, and was also elected a Fellow of the Royal Society of Tropical Medicine. He did a great deal to assist and guide the treatment of leprosy in mission hospitals throughout the Republic. But his greatest and most enduring service to these sufferers is undoubtedly the national policy which he succeeded in establishing for their treatment. Whereas the American

policy of compulsory segregation at Culion in the Philippines was accompanied by a rapid spread of the disease owing to concealment of early cases, Maxwell determinedly advocated one of free treatment in out-patient clinics with voluntary settlements only for the more severely affected patients. His prestige and reputation were so effective that this method has been adopted for the whole of China, with the result that all over the country patients with early infections are increasingly coming up voluntarily for treatment. In 1937 he published "Leprosy: A Text-Book for Use in China", which is at present being revised and translated into Chinese.

In 1923 he was called to Shanghai as executive secretary of the China Medical Missionary Association to handle a situation which was becoming critical. This association ever since 1887 had practically been the representative of modern medicine in China (Chapman, 1948); but it was now thought that, with the steady increase in the number



James Laidlaw Maxwell.

of well-qualified doctors outside the missionary ranks, its scope should be enlarged. Accordingly, under the new title of "China Medical Association", in 1925 it opened its membership to all western practitioners and to a few leading Chinese.

But there had already been founded by the foremost Chinese modern doctors in the country a rival National Medical Association, whose members began to urge that the China Medical Association membership should all be absorbed into their own organization. In the atmosphere of resurgent nationalism of those years it was a ticklish situation which perhaps no one except Maxwell could have handled. But with his wide friendships and high standing among the leaders on both sides, and his disarming tact and reasonableness, he was able in 1932 to arrange that both organizations should unite into one "Chinese Medical Association". In 1933 the membership of the combined association was 1700, and in 1941 it had grown to 3340, united in the friendliest professional solidarity and good fellowship. This weathered unshaken the anti-foreign feeling aroused by the 1926-1927 revolution, and has been of the greatest value in the last two years as the Government's attitude towards foreigners has steadily hardened. It was an achievement of no mean order.

Maxwell was elected the first executive secretary of the United Chinese Medical Association and was editor of the English edition of the *China Medical Journal* and later of *The Chinese Medical Journal*, from 1925 to 1933. From 1929 to 1936 he was also head of the Department of Field Research, and librarian, of the Henry Lester Institute of Medical Research in Shanghai.

From the foundation of the Chinese Medical Association Maxwell had been the secretary of its Medical Missionary Division, in which capacity he did a great deal to foster the corporate fellowship and interests of the two hundred odd mission hospitals in the country. One special feature of this activity was the training of laboratory technicians, who are in much more urgent demand in China than in Australia. During his service with the Royal Army Medical Corps Maxwell had demonstrated what excellent work could be done by picked young people after a short intensive practical course in laboratory technique; and in the early 1920's he lent all his influence to assist in the founding of a China Medical Association "Institute of Hospital Technology" for this and other technical training. In 1937, when this institute was training for hospitals over the whole country, he went to Hankow as its director.

Just at this time the Sino-Japanese War broke out, with its widespread devastation and destruction, and Maxwell was set aside to organize, in cooperation with the British Consul, the Hankow International Red Cross Committee, which collected large sums of money from all over the world for war relief throughout inland China. Its two chief activities were distribution of funds to feed famine-stricken refugees, and the provision of certain supplies and apparatus and a *per capita* subsidy to hospitals treating wounded soldiers. But for this assistance many of them would probably have had to close down. For this service he was created a Companion of the Most Excellent Order of the British Empire.

In 1940, after the Japanese had occupied Hankow, he returned to England and acted as *locum tenens* at Flitwick in Bedfordshire, releasing a medical practitioner for war service. In 1949, at the age of seventy-five years, after a recent prostatectomy, he offered with the utmost simplicity to go back to China just as the Communists were surging south. He wanted to take the place of a young doctor whose health had broken down at the Hangchow Leprosy Hospital, and to start a new project of the Mission for Lepers for an agricultural leprosy settlement twenty miles further north.

He and his wife, two years older than himself, arrived there and began work three weeks before the Communists' arrival, and there they carried on for the next two and a half years.

During this time he established the new settlement, gathered a Chinese Christian staff to run it, made a careful study of the results of the new sulphone therapy, and so directed the work that he won the whole-hearted support of the local Communist authorities. Although the specifically religious features of the two establishments were steadily and openly maintained, the Communists showed them the greatest friendliness, sent them many patients and supplied free rice for all the patients. And when everywhere else missionaries were being turned out of the country, they did their best to persuade Maxwell to remain permanently in charge.

However, he felt that his work for China was now done and made arrangements finally to retire from the field. He died a few days before he was due to sail. Thus ended, as he would have wished, his record of fifty years of brilliant and devoted service to the science of medicine, to the whole medical profession of China and, above all, to the Chinese people, whom he loved and for whom he laid down his life.

The People's China, the Peking Government's official English language fortnightly magazine, published an appreciative obituary notice, an extraordinary incident in these days of anti-foreign propaganda, and a "Maxwell

Foundation" is being set up by some of his British friends and colleagues to contribute to the maintenance of the Hangchow leprosy enterprise, his last bequest to China.

Reference.

Chapman, H. O. (1948), "The Organizaion of Modern Medicine in China", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, page 11.

Reports of Cases.

ACUTE LOCALIZED TERMINAL ILEITIS OF UNKNOWN ÆTIOLOGY.

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THE small bowel may be affected by many varied acute inflammatory diseases. The ætiology of some is known, as for instance the common ones due to the Salmonella infections or the rare ones due to the pyococci—the acute phlegmonous jejunitis or ileitis described by Brynjulfsen (1948). The ætiology of others is unknown, but they form definite, if uncommon, clinical entities. Here may be included the acute forms of Crohn's disease and the primary non-specific ulcers of the small intestine (Morrin, 1931; Evert, Black and Dockerty, 1948).

Here are reported two cases of acute localized terminal ileitis of unknown causation which, clinically and pathologically, differed from all the above-mentioned processes. This entity must be uncommon because Case II was the only one of its kind that has been recorded at The Royal North Shore Hospital of Sydney in the past twenty-six years; nor could any similar case be found in the available literature.

Case I.[1]

The first case is one of acute inflammation of the terminal part of the ileum of unknown ætiology causing necrosis of bowel and death of the patient.

A male Papuan native, aged twenty years, was admitted to hospital in New Guinea during World War II with the diagnosis of acute appendicitis. The presenting symptom was severe generalized abdominal pain for six hours. There was no vomiting or diarrhœa.

The patient was very ill with a furred tongue, a temperature of 102° F., a pulse rate of 100 per minute and a respiratory rate of 30 per minute. The abdomen had slight generalized distension. It was generally tender and rigid, these signs being most marked in the right iliac fossa.

Operation disclosed much serosanguinous fluid in the abdomen with intense inflammation and thickening of the distal eighteen inches of the ileum. The mesentery was not affected, nor were its lymph nodes enlarged. The blood supply to the bowel was normal. The appendix was normal.

The abdomen was closed immediately. The patient died three days later in a state of toxæmia with a paralytic ileus, in spite of all treatment including the administration of penicillin, gastric suction and intravenous alimentation.

An autopsy disclosed all systems to be normal except the gastro-intestinal tract, in which the jejunum was greatly dilated. The ileum was intensely injected and its coils were matted together with fibrinous adhesions. Subserosal hæmorrhages were present in the ileum and its lowest coil appeared gangrenous. There was no leakage of intestinal contents. The lymph nodes in the submucosa of the ileum were enlarged, but there was no submucosal ulceration. The mesentery was normal and the lymph nodes were not enlarged. No mechanical cause of an intestinal obstruction was present. Later, microscopic examination revealed only signs of acute non-specific inflammation and necrosis of bowel wall with a predominance of small round cells. No cultural examinations could be made owing to service conditions at that time.

[1] Previously reported in *The Australian and New Zealand Journal of Surgery* (Rose, 1946).

Case II.

The second case was one of acute inflammation of the terminal part of the ileum of unknown ætiology, leading to perforation and general peritonitis. Recovery of the patient followed suture of the perforation.

The patient, a Merchant Navy officer, aged twenty-five years, was admitted to The Royal North Shore Hospital of Sydney on January 8, 1948. His history was that shortly after leaving Mauritius six weeks previously he had had severe frontal headaches. For the six days prior to admission to hospital he had suffered in addition from shivers and sweats and generalized "hot and cold feelings" every two or three hours, especially at night. These were accompanied by loin pains. The exhibition of quinine and sulphadiazine on board ship was without avail. Just prior to admission to hospital he had had an attack of generalized mild colicky abdominal pain radiating to the right iliac fossa. This lasted three hours and culminated in diarrhœa, which relieved the pain.

Examination revealed a well-built sick young man. His tongue was heavily furred, his temperature was 102° F., his pulse rate was 100 per minute and his respiratory rate was 25 per minute. His systolic blood pressure was 120 millimetres of mercury and his diastolic 80 millimetres.

The abdomen was slightly distended and there was generalized tenderness but no rigidity. The spleen was just palpable, tender and soft. There was no rash or enlargement of lymph nodes.

There was no abnormality detected in any of the other systems. A urine analysis result was normal.

A full blood count showed a normal red cell count and hæmoglobin estimation. There were 9300 leucocytes per cubic millimetre, of which 51% were neutrophile cells, 30% lymphocytes and 19% monocytes. No malarial parasites were seen.

The patient's condition gradually worsened, and on January 13 he appeared very ill. His lips were covered with sordes and his tongue was heavily furred. The temperature was swinging between 101° F. in the morning and 104° F. at night. He still had attacks of mild abdominal pain and diarrhœa. The white cell count had fallen to 5250 per cubic millimetre, with 30% of neutrophile cells, 50% of lymphocytes and 20% of monocytes.

On January 14, six days after admission to hospital, he first complained of severe continuous generalized abdominal pain. This made him nauseated, and six hours later he vomited. Examination then showed the abdomen to be more distended and the generalized tenderness to be greater. However, there was still no rigidity. The spleen was no longer palpable. The patient looked exactly as if he had typhoid fever, though the serological tests failed to confirm this impression.

On January 15 the tenderness had localized to the right iliac fossa, where the muscles were rigid to palpation. The clinical impression was now that of a ruptured typhoid ulcer, and laparotomy was immediately performed.

Operation.—The abdomen was opened by a paramedian incision, the patient being anæsthetized by "Pentothal" supplemented by "Eulissin". The abdominal cavity was found to be full of foul yellow pus, from which *Bacterium coli* was grown on culture later. Three inches from the ileo-caecal valve was a very thickened, reddened area of

ileum four inches long. In the centre of this was a ragged perforation half an inch in diameter. The tissues round the perforation were no more thickened than the rest of the inflamed area. There was no involvement of the mesentery or its lymph nodes. A snipping was taken from the edge of the perforation and shown later to have the histological picture of an acute non-specific inflammatory process. A culture from this area showed *Bacterium coli* only. The appendix was normal.

Convalescence.—The patient gradually improved, aided in the first week by intestinal intubation, intravenous alimentation and antibiotics (penicillin and aureomycin). A small *Bacterium coli* abscess appeared on the wound, which, however, soon healed. The patient had diarrhœa for one week, and then the bowels acted normally. The temperature remained elevated for one month, slowly subsiding all the time. He left hospital on February 28, the full blood count being normal.

Course of the Temperature during the Illness.—The temperature daily swung from 101° F. in the morning to 104° F. in the evenings from his admission to hospital to operation eight days later. For the first four post-operative days it ranged from 99° F. to 102° F. For the next three weeks it ranged from normal to 101° F. and then gradually fell to normal over the next week.

Additional pathological investigations were performed. Widal tests against typhoid and paratyphoid organisms yielded repeatedly negative results, as did blood cultures for organisms. Cultures of fæces and urine failed to reveal any pathogenic organisms. The results of agglutination tests against *Brucella abortus* and typhus organisms (*Proteus XK* 19 and *OXK*) were always negative .

Follow-Up.—In December, 1950, almost three years after his illness, the patient wrote from the West Indies to say that he was very well. He had had no recurrence of his illness.

Comment.

On summarizing the above cases we see that, in the first instance, each was characterized by a severe general toxæmia-like reaction. This was followed by signs of acute inflammation of the terminal part of the ileum, which were confirmed both macroscopically and microscopically. The first patient rapidly died with the toxæmia and necrosis of bowel, whereas the other recovered, though not until ulceration of the affected area with perforation into the general peritoneal cavity had ensued. The toxæmia of this latter patient was such that clinically he resembled a sufferer from severe typhoid fever, even to the enlarged palpable spleen and leucopenia.

Consequently, this rare inflammatory process of the terminal part of the ileum must be thought of as a distinct disease entity commencing as a generalized infection, later localizing in the terminal part of the ileum.

No light is thrown on the ætiology, and it appears to differ from acute phlegmonous caecitis (Meyer and Disch, 1945), which does not have the severe constitutional reaction and is said to commence as a streptococcal or staphylococcal submucous infection (Spivack and Busch, 1943).

This disease is distinct again from that of acute Crohn's disease affecting the terminal part of the ileum, which has a benign course with less constitutional upset and shows pronounced involvement of the mesentery and its lymph nodes (Rose, 1946).

Nor is this disease akin to the primary acute non-specific ulcer of the small intestine (Morrin, 1931; Evert, Black and Dockerty, 1948; Shea, 1951) or of the caecum (Rosser, 1944; Lipton and Reisman, 1951). These ulcers cause very few symptoms save for vague abdominal pain until the complications of perforation or hæmorrhage ensue. The ulcer is then found to be a defect in the mucosa and deeper layers of the small intestine (or caecum) with well defined boundaries and little or no surrounding inflammatory reaction, which is a quite different picture from that presented in the two cases here described.

Serological tests will differentiate the Salmonella infections, and in cases in which perforation occurs culture from the ulcer may show the specific organisms of typhoid or paratyphoid fever (Kater, 1951). In these latter diseases also, the inflammatory process is not so localized and there are numerous ulcers.

When operation is necessary, snippings from the edges of these ulcers should always be examined microscopically; for example, in a case of a perforated terminal ileal ulcer which presented a macroscopic picture not unlike that seen in Case II, microscopic examination revealed the presence of an adenocarcinoma, which was shown at later autopsy to be a metastasis from a small asymptomatic primary renal carcinoma arising in the left kidney.

Treatment.

As one does not know the ætiology, treatment therefore can be only empirical, except for the complications such as a perforation.

In Case II the patient was too ill to allow resection of any bowel, and as it turned out, suture was all that was necessary, the patient being well and symptom-free three years later. Unfortunately the patient cannot now be traced for a later follow-up, so that one can only speculate as to later prognosis.

It would have been interesting to see what would have happened in Case I if resection of the affected area had been carried out. At the time of operation the patient appeared far too ill for such a procedure and one had the thought that perhaps the condition would settle down like acute Crohn's disease.

Summary.

Two cases of an entity characterized by a severe general constitutional disturbance ending in acute ileitis of unknown ætiology are presented and discussed.

In one case the patient died of toxæmia under a conservative régime. In the other the patient developed an ulcer of the terminal part of the ileum, which perforated into the general peritoneal cavity and caused peritonitis. Recovery ensued after simple suture of the perforation.

These cases are compared and contrasted with other lesions of the terminal part of the ileum, namely, the Salmonella infections, acute Crohn's disease and acute non-specific ulcer of the small intestine. As a consequence, this entity is shown to be different from all these.

Acknowledgements.

I wish to thank Dr. Wallace Freeborn, General Medical Superintendent of The Royal North Shore Hospital of Sydney, for permission to examine the records. I also wish to thank Dr. Innes Brodziak, senior physician of The Royal North Shore Hospital of Sydney, under whose care this patient was originally admitted.

I am indebted to Miss D. M. Drake, of the Unit of Clinical Investigation, for her clerical help in the preparation of the manuscript, and to Miss A. Scougall, librarian to the Institute of Medical Research, for her aid with the literature.

References.

Brynjulfsen, B. (1948), "Jejunitis Acuta—Ileitis Regionalis Acuta", *Acta chirurgica Scandinavica*, Volume XCVI, page 361.

Evert, J., Black, B., and Dockerty, M. (1948), "Primary Non-Specific Ulcers of the Small Intestine", *Surgery*, Volume XXIII, page 185.

Kater, N. (1951), "Perforation of the Ileum Amongst Prisoners of War in Korea", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 882.

Lipton, S., and Reisman, E. (1951), "Simple Ulcer of the Caecum", *Annals of Surgery*, Volume CXXXIV, page 279.

Meyer, L., and Disch, R. (1945), "Acute Phlegmonous Cecitis", *The American Journal of Surgery*, New Series, Volume LXVIII, page 398.

Morrin, F. (1931), "Spontaneous Perforation of a Primary Jejunal Ulcer", *The Irish Journal of Medical Science*, Volume II, page 198.

Rose, T. (1946), "Acute Regional Entero-Colitis with a Report of Three Cases", *The Australian and New Zealand Journal of Surgery*, Volume XV, page 184.

Rosser, C. (1944), "Simple Penetrating Ulcer of the Cecum", *Annals of Surgery*, Volume CXXXIV, page 279.

Shea, P. (1951), "Non-Specific Ulcer of the Small Intestine", *The Journal of the American Medical Association*, Volume CXXXVI, page 1490.

Spivack, A., and Busch, I. (1943), "Phlegmonous Cecitis", *The American Journal of Surgery*, Volume LXI, page 54.

SUBACUTE BACTERIAL ENDOCARDITIS CAUSED BY ERYSIPELOTHRIX RHUSIOPATHIÆ.

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ERYSIPELOTHRIX RHUSIOPATHIÆ, the causal organism of swine erysipelas, was described by Loeffler in 1882 (Wilson and Miles, 1946). Wilson and Miles state:

> It is possible that the bacillus observed four months previously by Thuillier (Pasteur and Thuillier, 1883) in pigs dying of rouget was the same organism as that described by Loeffler, but this is not absolutely clear.

A similar bacillus had been found by Koch in 1880 in the blood of mice that had been injected subcutaneously with putrefying blood.

Swine erysipelas affects mainly pigs, but infections have occurred in sheep, horses, cattle, turkeys and peacocks and possibly in fish. Four clinical types of infection of swine are recognized, the acute or septicæmic form, the urticarial form or "the diamonds", the chronic or cardiac form and the arthritic form.

The bacillus has also caused erysipeloid and endocarditis in man. Infection due to *E. rhusiopathiæ* was described by Rosenbach (1909) in 1884, and according to Klauder (1932) can always be traced to contact with animals, fish, shellfish, dead matter of plant or animal origin, or material derived from animals such as hides, pelts, bones and manure. It occurs in those who handle meat, fish, game or cheese—for example, butchers, fishermen and cooks—and is therefore justifiably to be considered as an occupational disease. By far the commonest type of the disease in man is the cutaneous form known as erysipeloid, but generalized infections have occurred. Klauder (1938) published a clinical analysis of 100 cases of erysipeloid, 88 of which had been caused by injury occurring in the course of employment. In 1940 Russell and Lamb (1940) described a fatal case of endocarditis caused by *E. rhusiopathiæ*; treatment with sulphanilamide had no effect upon the illness. Penicillin was of course not known in 1940. The diagnosis was established by bacteriological studies and confirmed at autopsy. A second fatal case of endocarditis was reported by Klauder and his associates in 1943. The patient was a retail butcher who cut his finger while working. Treatment with sulphathiazole was without effect; penicillin was not available. The organism recovered from blood culture was identified after death as *E. rhusiopathiæ*. Heilman and Herrell (1944) showed that penicillin was effective in the treatment of experimental infections and that it inhibited the growth of the organism *in vitro*. Barber, Nellen and Zoob (1946) described five cases of erysipeloid; the diagnosis was established bacteriologically and three of the patients were treated with intramuscular injections of penicillin, which appeared to effect a complete cure in forty-eight hours.

Sheard and Dicks (1949) described skin infections resembling erysipeloid during an examination of 43 fishermen at the Abrolhos Islands, Western Australia. Organisms resembling *E. rhusiopathiæ* were grown, but the work was carried out under field conditions and the bacteriological studies were not complete. MacDougall (1941) reviewed 30 cases of erysipeloid occurring in hospital out-patient practice and advised that systemic penicillin therapy should be used in all cases and continued until the lesion desquamated.

Clinical Record.

The patient, K.W., a male, aged twenty-two years, a butcher, was first admitted to the Royal North Shore Hospital of Sydney in 1945, when a diagnosis of rheumatic fever was made and he was in hospital for four weeks. After discharge from hospital he was in good health for the next four years. He was then admitted to hospital for the second time complaining of pain and swelling of several joints. On this occasion the diagnosis was rheumatic fever and patent interventricular septum. He was in hospital for five weeks.

After discharge from hospital he was well until a week before his third admission (on August 14, 1950), when he noticed shortness of breath on exertion, such as walking. This had become progressively worse, in that the distance travelled before breathlessness was noticed became shorter. At the time there was swelling of the knees and ankles, with a heavy feeling in the legs, unaccompanied by pain. There was some pain at the left sternal border on effort but no other symptoms.

On examination the patient looked healthy. His temperature was 100·4° F. and his pulse rate 104 per minute; these rose next day to 103·4° F. and 120 per minute respectively. The same figures were recorded on the third day. Thereafter, as a provisional report on blood culture had been received, treatment with penicillin was instituted, and pulse rate and temperature returned to normal and remained so. The blood pressure was normal. The heart was enlarged, and a thrill could be felt at the left of the sternum over the third, fourth and fifth ribs. There was a loud, harsh systolic murmur replacing the first heart sound, maximal in the third left intercostal space near the sternum. It was audible in the neck, on the right side of the chest and in the back on the left side of the spine. The second sound was clear. There was slight œdema in the region of the ankles. The spleen was palpable one finger's breadth below the left costal margin.

Laboratory Tests.

There were red blood cells in the urine and a moderate number of leucocytes, but the culture medium was sterile after forty-eight hours. The blood count showed moderate anæmia: the hæmoglobin value was 9·4 grammes *per centum*; red cells numbered 3,130,000 per cubic millimetre and leucocytes 9000 per cubic millimetre, of which 81% were neutrophile cells. The electrocardiogram was normal. Blood cultures made during the initial fever showed a small Gram-positive bacillus. The diagnosis was subacute bacterial endocarditis with defective interventricular septum. The patient was treated with intramuscular injections of penicillin, 500,000 units every six hours for twenty-eight days, after which time he was well.

Examination of the blood on October 4, 1950, showed 4,880,000 red cells per cubic millimetre and a hæmoglobin value of 14·7 grammes *per centum*. There were no red blood cells in the urine, and only an occasional leucocyte was seen. The patient has remained well since leaving hospital.

Identification of the Infecting Organism.

As mentioned above, each of three blood cultures, two made on August 14 and one on August 15, yielded a growth of a small bacillus, at first thought to be Gram-variable but later shown to be Gram-positive. After twenty-four hours' incubation on blood agar there was a moderate growth of flat, greyish-white colonies; after forty-eight hours' incubation small zones of slight, partial β hæmolysis were seen. Subsequent study of the organism established its identity on the basis of the following characteristics:

Morphology.—The organism was transferred from the blood culture to a blood agar plate and subsequently to broth, from which it was carried to glucose agar, McConkey's medium, tomato peptone agar and blood agar. When grown on blood agar the organism was a slender rod, Gram-positive, non-motile, non-sporing and non-acid-fast. Its diameter did not exceed 1μ and its average length was 2μ to 5μ within the range 2μ to 10μ. There were many irregular forms, and some were curved; in arrangement there was a tendency to palisade-formation. In colonies from a glucose agar plate,

the organism was more filamentous and measured up to 30μ in length. No growth occurred on tomato peptone or McConkey's medium. In glucose broth the morphology was rather similar to that on blood agar. Films prepared from agar cultures of the organism, as recovered from experimentally infected mice, showed tangled, hair-like, filamentous masses.

Cultural Characteristics.—After twenty-four hours' incubation on blood agar there was a moderately heavy growth of flat, conoidal colonies with an entire edge, grey-white in colour, homogeneous in structure and with a somewhat smooth surface. The blood showed a slight α change. After forty-eight hours' incubation the colonies were slightly larger and denser, and there was a slight partial β hæmolysis. The change in the blood medium, however, was somewhat inconstant, on one occasion resembling the α, on another the β, change. On glucose agar the appearances were similar to those on blood agar, but the colonies tended to be more irregular in form and with a mat surface.

Fermentation and Other Biochemical Reactions.—Fermentation reactions were rather slow in declaring themselves, were somewhat ill-defined and were inclined to be variable. They were as follows: glucose, *a* to (*A*);[1] lactose, negative to (*A*); fructose, *a* to (*A*); galactose, negative to *a*; inulin, doubtful *a*. There was no fermentation of maltose, sucrose, raffinose, dulcitol, mannitol, starch, dextrin, salicin or mannose. In milk there was no certain reaction. Gelatin was not liquefied; hydrogen sulphide was produced.

Animal Inoculation.—(i) A mouse was injected intraperitoneally with 0·1 millilitre of serum broth culture (forty-eight hours) containing about 1,000,000,000 organisms per millilitre. The animal was very ill by the third day and was killed. Examination *post mortem* did not reveal any very striking change. The heart blood was sampled aseptically and a culture obtained therefrom. In addition pieces of various organs were removed for histological examination. (ii) Another mouse was similarly injected with organisms derived from the heart-blood culture of the mouse in (i). This animal likewise was very ill on the third day (Friday) and died during the week-end. Both mice developed what appeared to be purulent conjunctivitis.

Histopathology of the Mouse Tissues.—(i) The distribution of microorganisms was as follows: In the heart, very many organisms were present between the muscle fibres, which seemed almost to be forced apart by the organisms. In the lung, numerous organisms were present, apparently within the capillaries of the alveolar walls. In the liver, organisms were somewhat scantily distributed. In the kidney, organisms were scantily distributed as in the liver, but considerable numbers were present in the perinephric fat. (ii) Histological examination revealed degenerative changes in the liver and in the kidney tubules; also the lung was intensely congested and had small patches of red hepatization.

Summary.

The history of a patient with subacute bacterial endocarditis due to *Erysipelothrix rhusiopathiæ* is presented. Treatment with penicillin was apparently successful. A brief account of some of the available literature is given.

Acknowledgement.

We wish to thank Professor H. R. Carne, of the University of Sydney, for checking the properties and identity of the organism.

References.

Barber, M., Nellen, M., and Zoob, M. (1946), "Erysipeloid of Rosenbach: Response to Penicillin", *The Lancet*, Volume I, page 125.

Heilman, F. R., and Herrell, W. E. (1944), "Penicillin in the Treatment of Experimental Infections due to Erysipelothrix Rhusiopathiæ", *Proceedings of the Staff Meetings of the Mayo Clinic*, Volume XIX, page 492.

Klauder, J. V. (1932), "Erysipeloid: Bacillus of Swine Erysipelas Infection—A Disease of Industry", *The Journal of Industrial Hygiene*, Volume XIV, page 222.

——— (1938), "Erysipeloid as as Occupational Disease", *The Journal of the American Medical Association*, Volume CXI, page 1345.

Klauder, J. V., Kramer, D. W., and Nicholas, L. (1943), "Erysipelothrix Rhusiopathiæ Septicæmia", *The Journal of the American Medical Association*, Volume CXXII, page 1938.

MacDougall, J. A. (1941), "Erysipeloid of Rosenbach", *The Lancet*, Volume I, page 1345.

Price, J. E. L., and Bennett, W. E. J. (1951), "The Erysipeloid of Rosenbach", *British Medical Journal*, Volume II, page 1060.

Rosenbach, F. J. (1909), *"Experimentelle, morphologische und klinische Studie über die krankheitserregenden Mikroörganismen des Schweinerotlaufs, des Erysipeloids und der Mäusesepsis"*, *Zeitschrift für Hygiene und Infectionskrankheiten*, Volume LXIII, page 343.

Russell, W. O., and Lamb, M. E. (1940), "Erysipelothrix Endocarditis: A Complication of Erysipeloid", *The Journal of the American Medical Association*, Volume CXIV, page 1045.

Sheard, K., and Dicks, H. G. (1949), "Skin Lesions among Fishermen at Houtman's Abrolhos, Western Australia, with an Account of Erysipeloid of Rosenbach", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, page 352.

Sneath, P. H. A., Abbott, J. D., and Cunliffe, A. C. (1951), "The Bacteriology of Erysipeloid", *British Medical Journal*, Volume II, page 1063.

Wilson, G. S., and Miles, A. A. (1946), Topley and Wilson's "Principles of Bacteriology and Immunity", Third Edition, London.

[1] *A* = maximum change in indicator colour due to fermentation.
(*A*) = lesser degree of *A*.
a = partial change only but regarded as indicative of fermentation.

Addendum.

Since the completion of this paper two papers bearing on this subject have appeared in the *British Medical Journal*. We should like to draw attention to them. They are those of Price and Bennett (1951) and Sneath, Abbott and Cunliffe (1951).

A CASE OF CARBON MONOXIDE POISONING TREATED BY REPLACEMENT BLOOD TRANSFUSION.

By B. J. IRELAND,
Resident Medical Officer, Saint Vincent's Hospital, Sydney.

THE patient, a woman, aged seventy-six years, was admitted into the casualty department in August, 1951; she was said to have been found in a gas-filled room. She was found to be deeply comatose, not responding to painful stimuli. Her colour was the normal fresh colour associated with carbon monoxide poisoning. Her plantar reflexes were extensor in type, but all other reflexes were normal, except for some exaggeration of the knee jerk on both sides. Her blood pressure was 120 millimetres of mercury, systolic, and 75 millimetres, diastolic, and the respirations were of Cheyne-Stokes character.

The usual methods of resuscitation were applied. "Carbogen" was administered and injections of "Coramine" were given. Three hours later the patient's condition was unchanged, and a replacement blood transfusion was decided upon.

During the next three hours replacement of four litres of the patient's blood was carried out. Difficulty was encountered in withdrawing the blood as rapidly as was desirable; 10,000 units of heparin were given intravenously to facilitate this. It being desirable to replace the patient's blood as quickly as possible, and the delay in this replacement occurring on the withdrawal side, venesection was given up, the radial artery was cut down upon, and a length of polythene tubing was inserted into the artery to keep it patent; this allowed a much faster rate of withdrawal, and consequently we were able to run in the fresh blood at a much faster rate. A qualitative carbon monoxide spectroscopic analysis was made before and after the transfusion, and in the post-transfusion specimen no carbon monoxide was present.

The patient's condition improved at the end of the transfusion, and within another hour she was responding to auditory stimuli. Her improvement over the next twenty-four hours was gradual; she was still confused at the end of that time.

Examined two days later, the patient was fully orientated and had as the only residual signs doubtfully extensor plantar responses.

The patient developed a severe bronchopneumonic condition despite prophylactic chemotherapy. Over the ensuing two weeks her convalescence was stormy, with pyrexial

exacerbations of the pulmonary infection. At this time an X-ray examination of the chest revealed some dulness at the base of the left lung, reported on as being probably either fluid or pleural thickening.

From this time the patient's condition gradually deteriorated. She became more and more drowsy and confused. Her blood urea level rose to 70 milligrammes *per centum* (microscopic examination of the urine gave results within normal limits). She maintained a fairly steady temperature between 101° F. and 102° F., and eventually died twenty-three days from the date of her admission to hospital.

At post-mortem examination an old infarct at the base of the left lung, and an ante-mortem clot in the main pulmonary artery were found.

Comment.

Although blood transfusion as a means of treatment in deep carbon monoxide poisoning is given a cursory mention in most text-books on theoretical grounds, I have found no evidence of its actual use for this condition.

It is indicated only for such patients as do not respond to the usual methods of treatment. Its only indications for use in this case were that after three hours the patient had failed to respond to the usually satisfactory methods of resuscitation and that carbon monoxide hæmoglobin was still present on spectroscopic examination.

Probably the outcome would have been more successful in a younger patient. If the pulmonary embolus was not the cause of death, then death was due to cerebral changes, which were probably those of old age accentuated by her anoxic experience.

Acknowledgements.

I wish to thank Dr. James Sherwood, honorary physician at Saint Vincent's Hospital, for permission to publish this case, Major R. J. Walsh, Director of the New South Wales Red Cross Blood Transfusion Service, for helpful advice during the carrying out of the procedure, and also the staff of the pathology department of Saint Vincent's Hospital.

Reviews.

RHEUMATIC DISEASE.

THE second edition of "Medical Disorders of the Locomotor System", by Ernest Fletcher, is a book whose previous excellent quality has been enhanced by the inclusion of four more chapters (over 200 extra pages) and additional authors.[1] The first six chapters form the foundation of the book upon which the rheumatic diseases can be scientifically presented. The chapter on the incidence of these diseases reveals many gaps in our knowledge as to prevalence in Great Britain, and the paucity of adequate survey is indicative of a greater need for statistical data. The ætiology of the rheumatic diseases is still not clear, but the facts as known today are ably presented, and focal infection receives the measure of ætiological value it merits.

The widespread pathology of these diseases is adequately shown, a broadening concept of their systemic nature being revealed. The author emphasizes the occurrence of acute rheumatoid arthritis with fever and sudden onset, a form of the disease which is moderately common and which may be difficult to diagnose.

The description of the variants of rheumatoid arthritis is a pleasing feature of the book, as it demonstrates the breadth of the rheumatoid problem, too long tenanted in narrow clinical compartments. Until the veil is drawn from the face of rheumatic ætiology, the author of this book rightly broadens the clinical picture of these diseases. Treatment of rheumatoid arthritis follows the present therapeutic trend.

[1] "Medical Disorders of the Locomotor System Including the Rheumatic Diseases", by Ernest Fletcher, M.A., M.D. (Cantab.), M.R.C.P.; Second Edition; 1951. Edinburgh: E. and S. Livingstone, Limited. 10" × 6½", pp. 896, with 377 illustrations. Price: 60s.

The author emphasizes the importance of chrysotherapy in the treatment of rheumatoid arthritis, but cortisone and ACTH receive the favourable comment that is now world-wide, the advantages and disadvantages of such therapy being adequately described. Physical therapy and orthopædic measures are given their requisite consideration in the therapy of this disease.

This book is a worthy addition to the library of the rheumatologist, can be recommended with great confidence to the general practitioner, is ideal for the young medical man who desires to specialize in rheumatology, and has a breadth of presentation of all phases of the rheumatic diseases which makes it a pleasure to read.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Antibiotic Therapy", by Henry Welch, Ph.D., and Charles N. Lewis, M.D., with a foreword by Chester S. Keefer, M.D.; 1951. Washington: The Arundel Press, Incorporated. 8½" × 6", pp. 576, with 8 illustrations and 34 text figures. Price: $10.00.

The purpose of the book is "to present in a concise, though reasonably complete form, the present status of the available antibiotics in the treatment of infectious diseases".

"The Book of Cancer Relief: Presenting an Outline of the Position Regarding Cancerous Diseases in Britain, and of the Forces Engaged in Combating the Scourge", with a foreword by the Countess Mountbatten of Burma, C.I., G.B.E., D.C.V.O. London: Katherine Evans. 10" × 7½", pp. 92, with a few illustrations. Price: 2s. 6d.

Intended for "the ordinary man and woman, and for young people of intelligence and purpose".

"Clark's Applied Pharmacology", revised by Andrew Wilson, M.D., Ph.D., F.R.F.P.S., and H. O. Schild, M.D., Ph.D., D.Sc.; Eighth Edition; 1952. London: J. and A. Churchill, Limited. 9" × 6", pp. 704, with 120 illustrations. Price: 37s. 6d.

First published in 1923 by A. J. Clark, the seventh edition was produced by him in 1940, one year before he died.

"La Spondylarthrite Ankylosante: Clinique, Radiologie, Anatomie Pathologique, Traitement", by J. Forestier, F. Jacqueline and J. Rotes-Querol; 1951. Paris: Masson et Cie. 10" × 7", pp. 334, with 143 illustrations. Price: 2650 Fr.

Based on the study of more than 400 cases, many of the patients having been followed over a period of many years.

"The Surgical Clinics of North America", 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Nationwide Number. 9" × 6", pp. 324, with 111 illustrations. Price: £7 5s. per clinic year (cloth binding) and £6 per clinic year (paper binding).

This is a "nation-wide" number. It comprises a symposium on minor surgery (18 articles on everyday subjects) and two additional articles. Dr. Michael E. DeBakey writes a foreword.

"Cleft Lip and Palate", by W. G. Holdsworth, F.R.C.S. (Edinburgh), F.R.C.S. (England), with a foreword by Harold Gillies, C.B.E., F.R.C.S.; 1951. London: William Heinemann (Medical Books), Limited. 10" × 7½", pp. 138, with 87 illustrations, a few in colour. Price: 35s.

An attempt to pose fairly the problem of cleft lip and palate and to bring it into true perspective.

"The 1951 Year Book of Obstetrics and Gynecology (August, 1950-June, 1951), edited by J. P. Greenhill, B.S., M.D., F.A.C.S.; 1951. Chicago: The Year Book Publishers, Incorporated. 8" × 5½", pp. 568, with 134 illustrations. Price: $5.00.

One of the "Practical Medicine Series" of year books.

"Clinical Laboratory Diagnosis", by Samuel A. Levinson, M.S., M.D., Ph.D., and Robert P. MacFate, Ch.E., M.S., Ph.D.; Fourth Edition; 1951. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9½" × 6½", pp. 1146, with 221 illustrations and 13 plates, 10 in colour. Price: £8 9s.

Intended for the student, the intern, the resident physician, the practising physician and the medical technologist.

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A COMMUNITY EFFORT TO CONTROL HEART DISEASE.

So many people at Newton, Massachusetts, held that heart disease constituted a public health problem that in May, 1948, the Massachusetts Medical Society approved of "a pilot study of the public health aspects of heart disease". The study was to be conducted at Newton under the joint sponsorship of the Newton Health Department, the Massachusetts Department of Public Health, and the United States Public Health Service. The first report of the study was presented at the annual meeting of the Massachusetts Medical Society in May, 1949.[1] In this report it was stated that the aims of the programme were: to analyse the extent of the heart disease problem in the local community; to analyse the present unsatisfied need of the potential and actual heart patient in the community; to evaluate the possible role of public health and other local agencies in meeting these needs; to obtain total physician-participation in the programme and encourage ever-increasing improvement in the quality of medical care; to develop a permanent all-out effort against the Number I killer of Americans. Some practitioners will be certain to regard a community effort such as this as unusual, if not unnecessary. It is therefore of interest to note that a report of three years' experience in the programme has been published.[2] The report was presented at the annual meeting of the Massachusetts Medical Society in May, 1951, and its authors are E. E. Kattwinkel, V. A. Getting, E. M. Morris and W. A. Zukel.

In the first report the first five requirements in the project were named. First of all, a well-informed medical profession was necessary. Secondly, information on the amount and kinds of heart disease occurring in Newton was needed. Thirdly, it was necessary to secure the participation of the public in order to ensure full use of community resources. In the fourth place, the study of the dietary needs of cardiac patients appeared to be necessary because nutrition touched upon many aspects of prevention and treatment. Finally, the rehabilitation needs of the patient required investigation if he was to receive full benefit from medical treatment. In the second report the authors state that they have learned that medical knowledge of the prevention of rheumatic fever and subacute bacterial endocarditis can be applied in a practical way in the community. They have also learned that several hospital services can be carried over into the community to help to delay the progress of heart disease and to prevent many unnecessary complications. Further, supplementary public health services in the community have enabled the medical practitioners of Newton "to provide the same excellent medical care for cardiac patients in the home that they provide for their patients in the hospital".

Some of the special points about this work may be considered in some detail. The post-graduate education of medical practitioners in this matter is evidently taken seriously. Lectures are given every month at the "Newton Post-Graduate Heart Institute" and the attendance is "sizable". At these gatherings stress is laid on the practical aspects of the management of the cardiac patient. Nearly half the time is spent in the answering of specific questions presented in writing by those attending. Summaries of the proceedings of each session are sent to every practitioner in the community. Unfortunately the reader of these reports is not told how large a place Newton is and there is no indication of the size of the population. The "sizable" attendances at post-graduate discussions must be looked on as satisfactory. Presumably this whole effort appeals to the imagination of the practitioners. The question of nutrition is mentioned, especially in regard to weight reduction of overweight persons suffering from hypertension or heart disease. It was found that most of these persons who lost weight as the result of discussion in group meetings had maintained their lessened weight or continued to lose weight still further. In order to simplify the problem of keeping a patient on a diet with a low sodium content, a booklet dealing with the subject was issued. The booklet is made available to the patient early through his medical attendant. By means of the book the medical practitioner is able to select a diet of a suitable level of sodium restriction. For those patients who have to use a restricted diet for the rest of their lives, a group education service for patients on a diet with a low sodium content has been established. This service is carried out by nutritionists connected with the heart programme, the hospital and the nutrition centre. Some interesting work is being carried out in the matter of rheumatic fever prevention. The recurrence of rheumatic fever in Newton was halted by the daily oral administration of penicillin and also by the advocacy of the immediate treatment of suspected streptococcal infection in members of the families of patients with rheumatic fever. To help the practitioner to confirm suspected streptococcal infection, throat culture studies were made free of charge. Penicillin was made available to physicians at cost price for members of rheumatic fever families. By means of a school survey about 350 Newton families were found to have a rheumatic fever history. The medical practitioners responded well towards this effort to prevent rheumatic fever. Some 50 children with rheumatic fever are now receiving special treatment from practitioners. This figure represented 80% of patients

[1] *The New England Journal of Medicine*, September 22, 1939.
[2] *Ibidem*, October 18, 1951.

known to have had rheumatic fever in Newton over the past five years. A year ago the percentage of such children receiving special care was only 16. No recurrences of the disease have been reported in any of the children who received penicillin. In order to study the effects of penicillin on the throat flora, throat-culture study was conducted on a group of 36 of the children in question with 36 controls. It was found that the children who received penicillin orally had significantly fewer positive cultures of β hæmolytic streptococci. In order to prevent subacute bacterial endocarditis, a programme was drawn up for use among persons with valvular or congenital heart disease who had to undergo dental or surgical procedures. Recommendations of the American Heart Association for the prevention of subacute bacterial endocarditis were combined with these recommendations. No cases of subacute bacterial endocarditis in persons undergoing dental or surgical procedures have occurred during the past year. The infrequency of this disease, however, makes it difficult to determine whether the measures adopted contributed to this good result. In the matter of case finding, it was found in the early stages of the programme that voluntary reporting of cases of heart disease was of little value. It was therefore discontinued. An effort was then made to discover persons with previously unknown heart disease or those with known heart disease who were not under medical supervision. It will be clear that any efforts to discover affected persons will have to be made with the greatest care if the establishment of a cardiac neurosis is to be avoided. It is claimed that the approach used has minimized the possibility of the creation of a cardiac neurosis and is regarded as having been moderately successful. The procedure consists of a seven-question, yes or no, cardiac history carefully taken; the height, weight and blood pressure are recorded and the heart is auscultated. So far, 5500 persons have been examined in this way and it has been found that 3% to 4% of those examined have heart disease or hypertension which was previously unknown. About an equal number of cases were previously known, but the patients were not under medical supervision. No information is given to the person examined in regard to positive findings. A report of the findings is rightly sent to the subject's medical attendant, who decides whether anything further is to be done. Some steps have been taken in rehabilitation of some patients with heart disease, but this work is apparently only in the early stages. Another report from Massachusetts deals with the findings of the review of minature chest films from the circulatory aspect, the work having been sponsored by the United States Health Service and the Massachusetts Heart Association. David D. Rutstein, Charles R. Williamson and Felix E. Moore have published two articles dealing with studies of the silhouette of the heart and great vessels on 70 millimetre films used in mass surveys for pulmonary tuberculosis.[1] The studies so presented are in two distinct groups, the first presenting the results obtained by a special team of radiologists working in pairs, who resurveyed all the films after the review for pulmonary disease had been completed, and reported on any abnormalities of the outline of the heart and great vessels. The authors admit that the posterior-anterior silhouette is far from ideal for the purpose of cardiac diagnosis, and that it cannot be used for the determination of the prevalence of cardiac disease, but they set out to find if the assessment of this shadow will identify a significant number of persons in a community who are suffering from some previously unrecognized heart affection. For the survey to be of any value it had to include a representative cross-section of the community, and also to be followed by an effort to get into touch with the suspected persons, so that the suspicion might be confirmed or otherwise, and some measure taken to benefit them. In all they examined 31,091 films, teams reading them for all abnormalities and for cardiac abnormalities. Of this total 1101, or 3·54%, were classed as abnormal, and of the persons represented 845 returned for further tests; 504 were found to be suffering from clinical heart disease. Two hundred and eighty of these persons were unaware of the existence of any such trouble. This group of "discoveries" represented 0·90% of the basic population. The numbers of people in this group increased with age, as might be expected, and the accuracy of the reading of the film also was greater in older persons. The results in the second group differed considerably from these. This group was made up of 99,791 films, of which 410 were classed as abnormal, 0·41% of the total. Three hundred and nine persons were further examined from this category, and 233, that is, 0·23% of the basic population, were found to have cardiac disease. Of this group of 233, 74 had no knowledge of their condition, that is, only 0·07% of the population. In this group as in the previous one, the precision of the reading of the films increased with the age of the patient. In both groups the commonest types of circulatory disease revealed by the surveys were hypertensive, combined hypertensive and arteriosclerotic, arteriosclerotic and rheumatic, in that order. David D. Rutstein also contributes an article in which he analyses the value of such screening procedures.[1] One important criterion is the yield of the procedure, and he thinks that comparison of the results with other forms of mass survey shows that the yield of previously unknown cases in the first group is satisfactory. This refers to the series in which the reading of the films was specially done for the purpose of uncovering possible cases of cardiovascular disease. He further thinks that estimates of cost would show such an inquiry to be worth while, although he points out that this particular inquiry was organized as a study, not as a routine mass survey.

The interesting thing about these reports is that they are presented with restraint. No extensive claims are made and those in charge of the programme are obviously content to hasten slowly. Subsequent reports will be awaited with interest.

[1] *Circulation*, November, 1951.

[1] *Ibidem*, November, 1951.

Current Comment.

THE PREVENTION OF ECLAMPSIA.

IN "The 1951 Year Book of Obstetrics and Gynecology" the editor, J. P. Greenhill, points out that "whereas pre-eclampsia is still common, eclampsia is becoming rare, in large cities at least, owing almost entirely to improved antepartum care". This statement, made by a well-known and experienced obstetrician conversant with the current

literature on the subject, forms a useful point from which to consider the work on eclampsia and pre-eclampsia at the Women's Hospital, Crown Street, Sydney, reported in the last three months. The first paper on the subject, that of T. Dixon Hughes, was read at the first Australian conference of Fellows and Members of the Royal College of Obstetricians and Gynæcologists in April, 1951, and was published in this journal on December 29, 1951. The second paper, by R. H. J. Hamlin, the medical superintendent of the hospital, was published in England early this year.[1] The third paper, by R. B. C. Stevenson, appears in this issue. Each paper presents a different point of view and to some extent different material drawn mostly from the common experience at the hospital. However, the one remarkable fact emerges: eclampsia has disappeared from the Women's Hospital, Crown Street, Sydney, and the incidence of severe pre-eclampsia is greatly reduced. Dixon Hughes states that in his private practice he had had 5000 deliveries without one case of eclampsia. With these results as an incentive similar standards of management were introduced into the Women's Hospital in 1948. As Hamlin has shown, the incidence of eclampsia at the hospital (for example, one case in 467 "booked" patients in 1947) was then of the same order as that of comparable hospitals in Australia, Great Britain and Eire. There were 102 cases among 36,700 "booked" patients during the years from 1936 to 1947, an average incidence of 1 in 350. By July, 1949, the situation was changed dramatically, and from March, 1950, until the time of compilation of these papers no case of eclampsia had occurred amongst "booked" patients at the hospital, the number of patients concerned being between 6000 and 7000.

No doubt there will be differences of opinion about the factors responsible for the results. The starting point was certainly the acceptance of the view, mentioned by Greenhill and now widely admitted, that antenatal care is all-important. The unique feature of the Women's Hospital work seems to be the remarkable thoroughness and attention to detail with which the antenatal care was carried out. There was much more than lip-service to the principles involved. The hospital staff, doctors, nurses, dietitians and almoners, accepted their share of the task conscientiously, and the amount of work done by the medical superintendent must have been prodigious. The object was to make antenatal care complete for all patients, it being realized that for a small number of patients to escape adequate supervision would create a serious flaw in the work. The results speak for themselves. On the methods of prevention and general antenatal care it is perhaps better to defer comment. Much stress is laid on the prevention of undue weight gain and on suitable diet, but uniformity of opinion on the relative importance of individual measures is not a conspicuous feature of the three papers. In essence the treatment has been empirical, as might be expected in view of the general ignorance of the essential ætiology of toxæmias of pregnancy. However, the details are recorded for those who will read them. It is to be hoped that others (and this needs to mean complete hospital staffs) will examine these three papers and try to achieve the same results. Then, as other and perhaps better controlled investigations are reported, we may begin to learn something about what pre-eclampsia and eclampsia are and to understand the rationale of the therapy responsible for this creditable achievement at the Women's Hospital.

THE DIAGNOSIS OF PHÆOCHROMOCYTOMA.

IT is customary to speak of a characteristic clinical picture of phæochromocytoma, its features resembling essentially those caused by an excessive dose of adrenaline. Particular stress has been laid on the paroxysmal nature of many of the signs and symptoms, especially the associated hypertension. It is now recognized that the hypertension may be persistent, and many cases of otherwise unexplained hypertension have been found (sometimes *post mortem*) to be due to phæochromocytoma without other notable diagnostic features. Thus, although clinical diagnosis can on occasion be relatively simple, clinical grounds are not always sufficient to indicate with certainty the presence or the absence of the tumour. Despite the appreciable operative mortality (a figure of 16% was quoted by G. F. Cahill and H. Aranow in 1949,[1] and it is much higher amongst children), and the occasional failure when a malignant tumour has metastasized or serious vascular damage has taken place, the results of surgical removal of the tumour are very satisfactory; cure appears to be complete in a large proportion of cases. For this reason accurate diagnosis is of particular importance. Most of the patients affected, according to R. H. Smithwick,[2] have a history of paroxysmal attacks of hypertension associated most commonly with headache, palpitation, vomiting and sweating. However, he points out, it is important to realize that some patients do not have these attacks, and may be regarded as having essential hypertension. In such cases unexplained rises in temperature, excessive sweating, a basal metabolic rate of + 20%, a raised blood sugar level and a rapid heart rate, particularly postural tachycardia associated with postural hypotension, should lead one to suspect the presence of a phæochromocytoma.

The main aspects of diagnosis (clinical, radiological, pharmacological) have been well surveyed in the paper by Cahill and Aranow already referred to, and in another place Aranow[3] has discussed the differential diagnosis, with particular reference to hypertensive patients in general. Aranow's view is that, whenever a patient has hypertension of obscure cause, whether it is persistent or intermittent, the presence of a phæochromocytoma is a possibility. If there is existent hypermetabolism and/or hypoglycæmia, this possibility is increased. Referring to patients with persistent hypertension, Aranow recommends than an active attempt to exclude the presence of these tumours should be made under the following circumstances: whenever any radical form of therapy, such as lumbo-dorsal sympathectomy or the "rice diet", is being considered for the treatment of the hypertension; prior to any non-emergency surgical operation; whenever evidences of damage associated with hypertension appear in cerebral, optic, cardiac or renal areas. Patients with persistent hypertension should always have pyelographic studies carried out before lumbo-dorsal sympathectomy is performed, but no special radiological search for neoplasms, such as perirenal air injection, is indicated unless other evidence suggests it. Patients with paroxysmal hypertension should undergo full radiographic studies, and it is well, in Aranow's view, to employ several of the provocative pharmacological tests. It would appear that the pharmacological tests are assuming increasing importance in the diagnosis of phæochromocytoma, and in the exclusion of that diagnosis; they are certainly gaining increasing prominence. This is not surprising, in view of the fallacies and difficulties associated with the clinical diagnosis. Radiological methods are useful and diagnostic in many cases, but their scope is limited, and perirenal air injections are, as R. H. Smithwick has pointed out, not without serious hazard.

This brings us to the assessment of the reliability of pharmacological tests. On this question attention may be drawn to two recent comprehensive articles,[4] one by J. A. Evans, H. J. Rubitsky, C. C. Bartels and E. C. Bartels, of the Lahey Clinic, and the other by G. Entwisle, C. A. Stone and E. R. Loew, from the Boston University School of Medicine. The report by Evans and his colleagues is concerned with the use and interpretation of diagnostic drugs and cold pressor studies based on their experiences in the hypertension service at the clinic over the past four years. Entwisle, Stone and Loew deal essentially with the

[1] *The Lancet*, January 12, 1952.

[1] *Annals of Internal Medicine*, September, 1949.
[2] *The Surgical Clinics of North America*, December, 1949.
[3] *The Medical Clinics of North America*, May, 1950.
[4] *The American Journal of Medicine*, October, 1951.

pharmacological basis of the tests. We shall refer here only to the main points raised. The drugs concerned can be divided into two groups: firstly, substances which cause or produce a typical attack and are especially useful in the paroxysmal form of the disease, being best fitted for use between attacks; secondly, the adrenergic blocking agents, which block the effects of adrenaline and/or nor-adrenaline released spontaneously or after some test procedure, and are especially suited to cases of persistent hypertension. In the first group histamine, "Mecholyl" and "Etamon" are considered, and in the second group "Dibenamine" and "Benzodioxane". From a review of the available literature and from their own laboratory experiments, Entwisle, Stone and Loew produce evidence to show that histamine and tetraethylammonium bromide probably induce attacks by a direct stimulating action on the adrenal medullary tissue. The mechanism of action of "Mecholyl" in inducing attacks is still not clear. It is thought that it may be due in part to direct stimulation of the chromaffin tumour and/or to reflex stimulation resulting from a preliminary fall in blood pressure. The adrenergic blocking agents apparently act by preventing the pressor responses to the circulating adrenaline and nor-adrenaline liberated from the adrenal tumours, but further detail of the mechanism involved is not yet settled. The study of Evans *et alii* is based on the response of 250 consecutive patients subjected to sympathectomy for hypertension, 20 patients with either labile or fixed hypertension for whom the diagnosis of phæochromocytoma was considered at some time, and four patients with clinically and pathologically verified phæochromocytoma. It is pointed out that patients in the group of pseudo-phæochromocytoma syndromes may present an almost complete text-book picture of phæochromocytoma clinically; consequently Evans and his colleagues believe that no patient should be subjected to exploratory operation without first having given an unequivocally positive response to one of the pharmacological tests, especially that with "Mecholyl". They lay some stress on the cold pressor response (the response of the blood pressure after immersion of the hand in ice water for one minute), because they believe that blood pressure "overshoot" in any of the provocative tests must exceed the cold pressor response before the blood pressure rise from the provocative tests can be considered significant. The administration of "Mecholyl", in a dose of 10 milligrammes by the subcutaneous route, is the best, safest and simplest screening test for all hypertensive and all normotensive patients in whom the diagnosis of phæochromocytoma is entertained. Evans *et alii* state that if one uses the term "overshoot" to mean any blood pressure reading exceeding the basal resting controls at the onset of a test, the test has over 98% reliability in the diagnosis of phæochromocytoma. If one accepts only "overshoots" greater than the cold pressor rise which occurs within thirty minutes after the onset of the test, the patient being not anæsthetized, the test assumes an accuracy of almost 100%. The results with histamine were much less reliable. Evans and his colleagues consider that histamine produces a positive result in the presence of phæochromocytoma by a similar mechanism to that of "Mecholyl", and it is the drug that has been most and longest used for tests of this nature; but in this investigation its administration resulted in too many "false positive" and "false negative" responses for it to be considered reliable by itself. With "Etamon" given intravenously in a dose of 300 milligrammes, 7·4% of "false positive" responses were obtained. Evans and his colleagues believe that a good hypotensive effect from "Etamon" is a fair pre-operative lability guide to the results that may be obtained by means of sympathectomy for hypertension, and should be used with that purpose in mind; any "overshoots" should only raise the suspicion of phæochromocytoma, and other pharmacological tests should be applied. Caution should be exercised with any patient suspected of having a phæochromocytoma who is given "Etamon". Of the adrenergic blocking agents, Evans *et alii* used "Dibenamine" and piperidylmethyl benzodioxane (933F). They found "Dibenamine" of considerable diagnostic help with certain patients who had sustained hypertension, although there was a 37% incidence of probably "false positive" results. It is considered useful also as a check on positive responses to provocative tests, by observation of whether or not the "overshoot" can be blocked, and in the prevention of hypertensive crisis with subsequent acute left-sided heart failure and peripheral hypotension during the operative manipulation and removal of a tumour. Benzodioxane was found to be of use in the assessment of three puzzling cases of pseudo-phæochromocytoma syndrome, but its use is limited to some extent by the pressor response which occurs, not only in the usual hypertensive syndromes, but also in cases of paroxysmal hypertension due to phæochromocytoma. It has the advantage over "Dibenamine" that the infusion itself takes only two minutes, so that blood pressure responses are more clear cut, but it is apparently specific only for adrenal medullary tumours associated with persistent hypertension.

ANGINA PECTORIS.

THE importance of certain forms of cardiac disease in the middle and later periods of life, in particular myocardial infarction, has perhaps diverted attention somewhat from the purely clinical syndrome of *angina pectoris*. In a detailed study of the hearts of persons who have during life evinced signs and symptoms of angina, P. M. Zoll, S. Wessler and H. L. Blumgart have defined for the purposes of their inquiry the nature of this syndrome.[1] They accept the term to denote a syndrome consisting of paroxysmal substernal or precordial pain or discomfort of short duration, frequently radiating to the shoulders and inner aspects of the arms, precipitated by exertion, emotion or other states in which the work of the heart is increased, and relieved by rest or nitroglycerine. For the purpose of record they regarded hypertension as being present if either the systolic or diastolic pressure was 150 or 90 millimetres of mercury respectively or higher. From 1101 unselected autopsies in which the hearts were injected by a standard technique these authors found they could build up a series of 905 cases in which adequate clinical observations were available, with the exception that in 35 the blood pressure records were incomplete. Among this series of 905 unselected cases there were 185 with a history of *angina pectoris*; 177 were accepted for study, eight being excluded in which the history existed for only a month before death. It will be seen that the controls available were adequate and further assured the adoption of an accurate and standard technique. The method adopted at autopsy was to inject simultaneously the left and right coronary arteries with differently coloured radio-opaque lead-agar material under pressure. The heart was then opened so that the major coronary arteries lay in one plane and X-ray examination was then carried out. With the film as guide the arteries were carefully dissected, and when full study had been made samples of tissue were taken from exactly localized areas of the heart for microscopic examination. All the vessels were carefully inspected for presence or absence of occlusion, narrowing, and intercoronary anastomosis, the last-named being demonstrated by the finding of injection material of mixed colours, the presence of injection masses distal to occlusions, and the proved existence of a continuous coloured endothelial channel between the two coronary systems. Further, the degrees of narrowing were estimated by graduated probes and classified accordingly. Other findings of major importance such as valvular disease or hypertrophy were duly noted. The most outstanding finding was that arteriosclerosis of the coronary arteries, together with narrowings and occlusions, was present in 90% of the series of 177 cases. Narrowing without occlusion was found in 51 out of the 177. Comparison with the clinical history showed that myocardial fibrosis was demonstrable in 90%, and intercoronary anastomosis in 88% of a specially selected series of 90 hearts. This smaller series was derived from 500 hearts in the entire series in which special microscopic

[1] *The American Journal of Medicine*, September, 1951.

sections were available; of these, 238 showed coronary occlusion or narrowing, and in 90 cases of this number there was a well-established history of angina.

In order to illustrate the connexion of clinical events with the demonstrated pathology, ten case histories are related in detail by the authors. One of these deserves brief mention by reason of the absence of any coronary artery disease or fibrosis, the only recorded abnormality being hypertension; it is of interest that well-marked intercoronary anastomoses were present. The authors add to the point of these clinical stories by appending a small diagram of the coronary circulation in each instance. Examination of the whole series showed that the sex ratio among the anginal group was predominantly male, 2·5:1, contrasting with 1·4:1 in the control series. Only seven of the patients with angina died before the age of forty years, and each of these seven had valvular heart disease. Of the anginal subjects 60% died from cardiac disease, the remainder died from extracardiac causes. A summary of the results of this research shows that no patient with an established history of angina was found to be free from pathological changes in the heart after death. Study of persons with various types of heart disease showed that 52% of those who had suffered from coronary occlusion had anginal symptoms, and 16% of those with valvular disease. More interesting still is the finding that 5% of those with coronary narrowing and 3% of those with hypertension had *angina pectoris*. Of course, it must be remembered that there are other extracardiac factors of significance in the production of the anginal syndrome. However, the connexion between the degree of coronary obstruction and the incidence of angina was indisputable; no fewer than 85% of patients with occlusions of the main three coronary arteries suffered from attacks of angina. The mortality rates show that one-third of the patients with angina were dead within a year of the onset, half within two years, three-quarters within five years and nine-tenths within ten years. No close application of these figures to clinical estimates of possible longevity is justified because they are derived from post-mortem evidence and a retrospective history. It is perhaps encouraging to learn that in this series an intercurrent episode of myocardial infarction did not shorten the expectation of life of the patients with angina.

The authors conclude that their work demonstrates the underlying mechanism of angina as a relative disproportion between the blood required by the heart and the supply its coronary system can provide. Their study has emphasized the clinical importance of the anginal syndrome, and the need for basing diagnosis and treatment on the known pathology. Further, since no prevision can guess when an episode of infarction may occur, it is well to help towards the establishing of Nature's response to ischæmia, an improved compensatory anastomosis.

CARDIAC CONDITIONS AND THE RISKS OF SURGERY.

WHEN a patient known or suspected to have some form of circulatory disease is faced with the risks of some major surgical procedure his physical state is naturally reviewed, so as to determine whether the responsibility of the surgeon is thereby significantly increased. This question can usually be answered by a careful study of the history of the individual patient and the appraisal of the routine clinical examination, without further elaboration. Whether the answer is given by a skilled specialist anæsthetist or by a physician particularly interested in cardio-vascular disease or by an experienced general practitioner, it requires careful thought, but not thought distorted by beliefs without sound foundation. A. Carlton Ernstene deals concisely with this subject in one of the "Clinical Progress" articles which are one of the features of the journal *Circulation*.[1] He refers to the common belief that anæsthesia and surgical operations subject the heart to a considerably increased demand for work, but points out that there is no evidence for this. What are the greatest risks of anæsthesia, for example? Anoxia is an important hazard, so, too, are arrest of the heart and ventricular fibrillation, though the two last mentioned are less significant in general since they are, fortunately, rare. Cyclopropane may induce cardiac irregularities, and also causes sensitization to adrenaline, but drugs requiring special care in administration require also the skilled hand. It is a truism that the anæsthetics chosen should be thoroughly understood by the anæsthetist. The avoidance of anoxia during anæsthesia is the problem of the anæsthetist also, and he is vitally interested in shock, though he cannot be held responsible for its appearance. Ernstene states the universally held view that as a general rule, if shock and anoxia are avoided, patients with organic heart disease who can perform ordinary daily activities without symptoms of inefficiency of the myocardium or the coronary circulation, will tolerate a general anæsthetic and a surgical operation as well as normal persons. Therefore the discovery of some degree of cardiac enlargement, or valvular disease, or disturbance of rhythm, will call for careful examination and in particular careful inquiry about the patient's activities, but need not veto surgery. An abnormal electrocardiogram really offers no greater difficulty as a rule, except that due to the peculiar aura which seems to surround such special technical methods. Congestive heart failure brings up a problem of its own. Ernstene points out that if operation is imperative to save life, then the risk must be accepted, but safety may be reasonably assured if the patient is brought under control by the administration of digitalis, if necessary by parenteral injection. The same applies to auricular irregularities to a considerable extent, and possible complications may be avoided by prompt digitalization. In those forms of heart disease in which sudden death is a possible, even if not imminent, event, surgery is best avoided, but the writer sagely remarks that if operation is really necessary, the risk must not be magnified beyond its true proportions. Statistics are quoted to show that cardiac death is uncommon in such subjects during or after operation. Recent myocardial infarction is considered as a contra-indication if postponement of operation is at all possible.

Those general remarks on surgery in the subjects of cardio-vascular disease contain no novelty, but the problems involved are frequently met, and therefore a little thought about them is valuable, particularly with regard to the principles involved. Nothing has been said about the post-operative risks, which need no special mention at present. In conclusion, however, it is worth while to go back to the first principles of cardiac physiology, and see how they apply here. The same journal pays a physiologist the compliment of producing a later issue in his honour. Carl J. Wiggers has devoted most of his life to the study of the physiology of the circulation, and contributes a review of the knowledge gathered over eighty years concerning the factors underlying cardiac performance.[1] His article traverses the researches of Bowditch in 1869, of Howell and Donaldson, of Henderson, of Starling, and of Straub, Katz and himself. He points out that, in spite of some alterations in findings and beliefs, the basic laws seem to stand as before. The ventricles will empty in accordance with their presystolic size, that is, they obey the general law of muscle, and produce energy of contraction in proportion to the length of fibre. Yet this applies only under equivalent states of responsiveness, and Wiggers stresses the importance of the various factors which influence the myocardium, a field awaiting further experimental and clinical study. As our knowledge stands at present we are reasonably well equipped to help the surgical patient who is also handicapped by heart disease. Progress in anæsthesia as a specialty has been remarkable during the last generation, and sounder concepts of shock have prevailed, particularly in its relation to blood loss, so we may rely with greater confidence on the handicapped though still competent cardiac muscle to carry on, provided we control those factors which may increase the burden.

[1] *Circulation*, September, 1951.

[1] *Circulation*, October, 1951.

Abstracts from Medical Literature.

OBSTETRICS AND GYNÆCOLOGY.

Sarcoma of the Uterus.

W. N. THORNTON, JUNIOR, AND J. P. CARTER (*American Journal of Obstetrics and Gynecology*, August, 1951) present a clinical study of sarcoma of the uterus based on 24 cases. They state that this condition comprises a heterogenous group of tumours of mesodermal origin, including leiomyosarcoma, endometrial sarcoma, mixed mesodermal tumours including the botryoid sarcoma of childhood, and angiosarcoma. In their series the ratio of sarcoma to fibromyoma was 1:102, and to carcinoma 1:66. Sarcoma was encountered once in every 106 hysterectomies. The tumours were grouped as to site of origin; two appeared to have originated in the endometrial stroma and 14 in the myometrium, six of these being in such association with a fibromyoma as to suggest its origin from this tumour. In eight cases classification was not attempted; three of the tumours were carcino-sarcoma and two were *sarcoma botryoides*. Twenty-two cases occurred in adults at the average age of fifty-four years, and two occurred in children. The most common presenting symptom was post-menopausal bleeding, which occurred in nine cases. Abdominal or back pain was the main complaint in four cases. In 17 cases the disease appeared after the menopause at an average interval of seven years. The disease was not suspected pre-operatively in any of the adult cases. Four of the patients had received intracavitary radium therapy for metro-menorrhagia more then ten years prior to the establishment of the diagnosis of sarcoma. Among adults the five-year survival rate was 8%; 19 of the patients were treated surgically, 10 by total hysterectomy and nine by subtotal hysterectomy. Of the two children with *sarcoma botryoides*, the condition of one was judged too advanced for treatment; the other, who received 4000*r* of X-ray therapy, was alive and well without recurrence three and a half years later.

Endometriosis.

R. E. FALLAS (*The Western Journal of Surgery, Obstetrics and Gynecology*, September, 1951) records an incidence of 150 cases of endometriosis in 388 consecutive laparotomies for pelvic disease in his private practice. He states that his experience agrees with that of other authors who consider that endometriosis is found more commonly in the private hospital class of patient than in the public wards. The association of infertility with endometriosis is borne out in the series analysed. Over one-third of the women in the group failed to become pregnant, only 52 children were born to this group and there were more than 27 abortions. The ages of patients ranged from twenty-three to sixty years, the highest incidence being amongst those aged between thirty and thirty-nine years. The lesions found at operation varied from small peritoneal implants to large chocolate cysts of the ovaries, and one or both ovaries were involved in 78% of patients. Acquired dysmenorrhœa and dyspareunia were the outstanding symptoms. The author states that typical symptomatology and advanced disease with abnormal pelvic findings may make the diagnosis easy, but the majority of cases of general pelvic endometriosis cannot be diagnosed pre-operatively with any accuracy. About two-thirds of the cases in this series were not diagnosed until the abdomen was opened. The author considers that this difficulty in diagnosis is likely to lead to fallacious results for treatment medically or by X-ray therapy without operation. Surgical treatment, either conservative or radical, is generally accepted as the treatment of choice. Of the patients in this series 56% were treated conservatively, some ovarian tissue being conserved. Results following conservative treatment were not quite as satisfactory as those after radical treatment. The author considers it reasonable to assume that the acquired dysmenorrhœa, dyspareunia and pelvic pain are due not to the original lesion of endometriosis, but to the massive dense adhesions which bind the pelvic organs together as the disease progresses. Hence, no treatment by hormones or X rays can be expected to do more than arrest the process at its advanced state. Surgery permits certain identification of the disease; its distribution can be appraised and a decision made regarding the desirability of radical or conservative surgery. Eighteen cases in the series were unconfirmed by pathological study, and the author makes a plea for closer cooperation between the surgeon and pathologist in order that laboratory verification of the diagnosis may be more often made.

Bilateral Polycystic Ovaries: The Stein Syndrome.

M. L. LEVENTHAL AND M. R. COHEN (*American Journal of Obstetrics and Gynecology*, May, 1951) summarize the literature on bilateral polycystic ovaries and the Stein syndrome since Stein's original work on this subject in 1929. They report a detailed analysis of another 10 cases from the Michael Reese Hospital over the four-year period 1945-1948. They state that the Stein syndrome is characterized by menstrual irregularity featuring amenorrhœa, a history of sterility in married women, the masculine type of hirsutism and, less consistently, retarded breast development and obesity. The ovaries are similarly and simultaneously enlarged, and show typical cystic changes, which are irreversible and refractory to hormonal therapy. The mechanism of the production of a pathological accumulation of cysts in the ovaries associated with fibrosis is not fully understood, but it is generally considered to be due to a pituitary-ovarian hormonal dysfunction. Experimental and histological work by Reynolds and Delson suggests that gonadotropic dysfunction may stimulate atretic follicles and that the spiral arterioles in the region of the follicles may become straightened; increased pressure in these arterioles results in a transudation of fluid into the follicles with the formation of an irreversible cystic growth. The diagnosis of bilateral polycystic ovaries with the Stein syndrome is made chiefly from the history of secondary amenorrhœa and sterility in married women. There are frequently no stigmata of gross endocrine abnormality, but hirsutism may be present in 50% of cases. Characteristic findings on pelvic examination are a normal or small uterus and associated bilateral enlargement of the ovaries. In patients who are obese or difficult to examine the enlargement of the ovaries may not be detected unless examination under anæsthesia or pneumoradiography is performed. The authors have found the condition unresponsive to treatment by thyroid medication and hormonal treatment. The pathological pattern of the ovaries is characterized by enlargement of the ovaries, a thick pearly white *tunica albuginea*, innumerable follicle cysts beneath the tunica and pronounced hyperplasia of the *theca interna* cells. *Corpora lutea* are usually absent, but luteinization is usually a feature of the *theca interna* cells. The authors think it probable that the hyperplastic *theca interna* layer present in polycystic ovaries may produce an excess of steroid, which inhibits true menstruation; possibly progesterone or one of its derivatives may exert androgenic effects. Of the patients in the ten cases analysed, six were married and four were single. Amenorrhœa varied from five months to four and a half years in the married group, and from five months to two years in the single group. Surgical treatment of the ovaries resulted in the restoration of a normal menstrual cycle in each case. Four out of five patients with sterility became pregnant after operation, and one patient had a recurrence of the condition one year after childbirth. Hirsutism was present in seven of the ten patients, and surgical treatment resulted in reduction of the hirsutism in four of these patients.

Anticoagulant Therapy in Gynæcological Surgery.

B. E. URDAN AND M. WAGNER (*American Journal of Obstetrics and Gynecology*, May, 1951) state that despite modern advances in medicine the danger of intravascular clotting and pulmonary embolus still persists and remains one of the dreaded complications of gynæcological surgery. They report a study of 900 consecutive major gynæcological post-operative cases. In 450 of these cases dicoumarol was given routinely as a means of preventing any untoward complications from intravascular clotting. The 450 patients were operated upon by the senior author, while the patients who were not given dicoumarol were treated surgically by both gynæcologists and general surgeons. Early ambulation was practised as a routine for the entire 900 patients. The authors state that the pharmacological effect of dicoumarol is to lengthen the prothrombin time by decreasing the prothrombin level of the blood. They employed the "simple bedside test" of Ziffren to determine the daily prothrombin level of the blood. They recognize that the safe and effective degree of prothrombin deficiency produced by dicoumarol in the blood is between 10% and 30% of normal, and that serious bleeding should not occur if the level of prothrombin is greater than 10% of normal. They consider that the requisites for adequate dicoumarol therapy are a reliable laboratory, daily determinations of prothrombin time and individualization of each patient. The entire twenty-four hour dose of dicoumarol was administered orally at about the same hour each day. The plan of dosage used by

the authors depended on the control prothrombin time determined on the morning of the first post-operative day. The daily dosage of dicoumarol varied from 300 milligrammes when the prothrombin time was 100% of normal to 100 milligrammes or less of the drug when the prothrombin time was below 60% of normal. The authors stress the importance of using the initial control prothrombin time as an index of dicoumarol therapy. They endeavoured to maintain the prothrombin deficiency at a level of 30% to 40% of normal by dicoumarol treatment until the patients were totally ambulatory for three days. They state that the hazard associated with the use of dicoumarol is hæmorrhage; seven cases of hæmorrhage were encountered in the series which were attributed to over-dicoumarolization. The drugs "Hykinone" and "Synkavite" act promptly in such cases of hæmorrhage and arrest bleeding in from four to twenty-four hours. Certain contraindications to dicoumarol treatment are listed by the authors. Among the 450 patients not treated with dicoumarol there were 31 complications associated with intravascular clotting. These comprised seven cases of phlebothrombosis, eleven cases of thrombophlebitis, nine cases of pulmonary embolism with infarction, and four cases of fatal pulmonary embolism. In the comparative group of 450 cases treated with dicoumarol, there was only one vascular complication, and this occurred in a patient who was refractory to dicoumarol and who developed phlebothrombosis. The authors consider that the prophylactic use of dicoumarol is safe and will decrease the incidence of, or entirely eliminate, intravascular clotting and its sequelæ.

Carcinoma of the Corpus Uteri.

M. B. DOCKERTY, S. B. LOVELADY AND G. T. FOUST (*American Journal of Obstetrics and Gynecology*, May, 1951) report a detailed study of 36 patients, less than forty years of age, with *carcinoma corporis uteri*. They state that these represent an incidence of 2·1% of a total of 1694 patients treated for *carcinoma corporis uteri* at the Mayo Clinic over the forty-year period 1905 to 1944. Fifteen of the 36 patients were less than thirty-five years of age, and 21 were in the age group thirty-five to thirty-nine years. There was a striking incidence of infertility noted by the authors in the series. Abnormalities of the menarche were not features, but practically all patients subsequently developed meno-metrorrhagia for periods varying from one month to twenty years. Among the patients with excess bleeding the authors noted ten patients with amenorrhœa of long or short duration. Leucorrhœa was present in ten cases, and in another ten cases the patients had complained of sterility or infertility. Patients with symptoms such as irregular meno-metrorrhagia, amenorrhœa and leucorrhœa were found to have been intractable to hormonal treatment, curettage of the uterus and implantation of radium. Thirteen of 32 patients investigated were obese, with weights in excess of 100 pounds, and three of the obese subjects exhibited hirsutism. Seven patients showed features of the Stein-Leventhal syndrome, and the authors consider that the possibility of carcinoma of the uterine corpus complicating this syndrome has not received sufficient emphasis. A high incidence was noted of associated fibromyoma, myohypertrophy, endometrial hyperplasia, cervical glandular metaplasia and cystic changes in the ovaries. The authors consider that this suggests the existence of chronic "hyperœstrogenism", but they have no direct evidence that such excess œstrogen activity is a fact. Pathologically, an increased incidence of malignant adenoma and adenocanthoma was noted. The authors consider that radium therapy previously given to some of these patients for the control of functional uterine bleeding did not appear to have induced the subsequent development of cancer, but it apparently failed to halt the later development of endometrial carcinoma. The ovaries were noticed to be large and cystic in 50% of cases in which total hysterectomy was performed, and in six cases the ovaries were covered by thick cortical rinds, under which lay a ring of follicular cysts. The authors focus attention on the clinical pattern of patients under forty years who develop endometrial carcinoma. They state that such patients may be obese and hirsute with high sterility and low fertility rates: hypertension is commonly present, and diabetes occasionally is a feature. Patients with the Stein-Leventhal syndrome may have an associated endometrial carcinoma. The authors consider that the treatment of choice is total abdominal hysterectomy followed by post-operative radiation therapy.

Vaginal Metastases of Carcinoma of the Body of the Uterus.

STANLEY WAY (*The Journal of Obstetrics and Gynæcology of the British Empire*, August, 1951) reviews reported cases of vaginal metastases of carcinoma of the body of the uterus from the literature and records 14 cases which he has encountered. From this he discusses the mode of origin of these vaginal metastases and their clinical significance and treatment. He states that *carcinoma corporis uteri* is not a common disease, vaginal metastases are rare, and knowledge of this subject is necessarily limited. The 14 cases of vaginal metastases occurred among a total series of 102 cases of *carcinoma corporis uteri*—an incidence of 13·7%. Of the patients 85% were in the age group of fifty to seventy years, and the age of the patient is not considered to have any special significance in relation to vaginal metastases. Thirteen of the 14 vaginal metastases were situated on the anterior vaginal wall underneath the urethra one centimetre from the introitus. The author considers that there is complete justification for the statement that the finding of an adenocarcinoma in the lower third of the vagina is diagnostic of carcinoma of the uterine body. The following histological features are noted: among 65 cases of adenocarcinoma of the body of the uterus were six with vaginal metastases; among 14 cases of mixed adenosquamous tumours were eight with vaginal metastases. Broders's grading was applied to these tumours, but appears to have been of little significance. Among the mixed tumours the difference in the proportions of squamous and adenomatous elements present in the primary and secondary growth was a feature. The author discusses the three possible methods of origin of vaginal metastases from corporeal carcinoma. Spread by implantation is considered most unlikely, and in the author's opinion is probably never a method of origin. Origin by retrograde lymphatic spread is more likely, but metastases of this kind are rare in cases of carcinoma of the cervix, a disease which is notorious for its frequent involvement of the lymphatic system. The author suggests that spread to the vagina by venous embolism is worthy of consideration for the following reasons: vaginal metastases are rare in cancer of the cervix, other blood-borne deposits are often found in cases of carcinoma of the body of the uterus, and other malignant tumours which often spread by the blood-stream (chorionepithelioma and hypernephroma) may metastasize to the vagina. In nine of the 14 cases studied vaginal metastases were present at the time when carcinoma of the body of the uterus was diagnosed; in four cases the metastases appeared after hysterectomy, and in one case the vaginal metastasis was present for twenty-one months before the diagnosis of carcinoma of the body of the uterus was made. In the author's series of 14 cases long survival rate is only 7%, and he considers that the bad prognosis supports the theory of spread by the blood vessels. He concludes that in all cases of carcinoma of the uterus with vaginal metastases the patient should have a radiological examination of the chest and skeleton. Hysterectomy and radiotherapy to the metastases would appear to be the correct line of treatment in most cases. Surgical measures aimed at treating the vaginal metastases should be radical and include removal of the urethra, transplantation of the ureters, hysterectomy, vaginectomy and cystectomy. The author considers that the finding of adenocarcinoma of the vagina affords immediate indication for cervical biopsy and uterine curettage. Even if curettage gives negative findings, hysterectomy should be carried out if no other contraindications are present. Finally, squamous carcinoma situated in the lower third of the vagina is an indication for uterine exploration.

An Anterior Pituitary Hyperhormonotrophic Syndrome.

BERNARD ZONDEK, Y. M. BROMBERG AND S. ROZIN (*The Journal of Obstetrics and Gynæcology of the British Empire*, August, 1951) describe a new syndrome in which three hormonotrophins are over-produced in the anterior pituitary lobe—the gonadotrophic, lactotrophic and thyrotrophic hormones. The resulting disease is manifested by prolonged, irregular and excessive uterine bleeding, galactorrhœa and thyrotoxic symptoms; there may also be a tendency to hypoglycæmia and secondary symptoms, such as physical exhaustion, secondary anæmia and secondary sterility. The authors report five cases of this syndrome and give clinical and pathological details. They state that the condition is rare and has been found in women in the age group of twenty to thirty years; no case has been observed in a childless woman. They consider that over-production of gonadotrophin leads to continuous stimulation of the theca cells in the follicle with continuous secretion of œstradiol. This acts on the uterus and breasts and also stimulates the thyrotrophic and lactotrophic factors of the anterior pituitary lobe.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

X.

RESPIRATORY INFECTIONS IN CHILDREN.

PARENTS seek medical advice about their children for many reasons, but for none so frequently as for infections of the respiratory tract. This is hardly surprising when one considers that the infant enters life with a negligible immunity to the many organisms he is bound to inhale.

Such infections present special difficulties to the physician when the child is inarticulate and the symptoms observed by the mother bear no relation to the respiratory tract. The toddler taken suddenly ill with fever and convulsions may have acute tonsillitis, while his elder brother, sharing a similar infection, may complain principally of nausea and abdominal pain.

The introduction of antibacterial drugs and the increasing knowledge of virus diseases have materially altered the attitude of pædiatricians. It was once enough to know the location and severity of an infection before proceeding to treatment that was generally palliative. Today one aims at the identification of the infecting organism in order to select from a variety of remedies that most appropriate to the case.

A single article cannot cover adequately all the respiratory tract infections to which children are prone. No reference will be made here to diphtheria, pertussis, measles and other contagious diseases, although the respiratory tract bears the brunt of the infection, and the discussion of other conditions will be chiefly confined to those clinical and diagnostic features wherein children differ from adults.

The Common Cold.

Adult and child are alike in the frequency with which they suffer from the common cold. In the first few years of life colds are often febrile. Thereafter they present the usual symptoms of an initial catarrhal stage of virus origin followed by a mucopurulent stage of bacterial invasion, unaccompanied by fever. The bacterial invaders, of which in the young infant staphylococci are the most important, are chiefly responsible for the spread of infection to other areas.

For anatomical reasons *otitis media* is a common complication in young children, showing its presence by such symptoms as fever, restlessness, crying and pulling at the ears. Routine inspection of the drums should never be omitted.

The parent's cold, accidentally conveyed to a newborn infant, may swiftly progress to bronchopneumonia, the shortness of the respiratory passages and the total lack of immunity contributing to this calamity.

One frequently hears the complaint that a child of five or six years is "never free from colds", and inquiry reveals that he is the eldest in the family or an only child. He has not inexplicably deteriorated in health, but is now facing—after a sheltered existence—the incessant coughs and sneezes of a crowded schoolroom. It has been calculated that the average immunity to a cold lasts only seven weeks, after which exposure becomes the all-important factor. There seems to be no evidence that chronic tonsillitis favours an excess of colds or that tonsillectomy confers protection from them. Coryza vaccines cannot give protection against the initial infection, nor do they appear to be of much avail against the secondary bacterial phase.

When confronted by a child with frequent "colds", one must consider allergic rhinitis. The presence of large numbers of eosinophile cells in the nasal secretion and pallor of the mucosa would be suggestive.

Although there is no specific treatment for a cold, aspirin in doses of one grain per year up to five years relieves the malaise and restlessness. Nasal drops of "Neo-Synephrine" (0·25%) or ephedrine (0·5%) in isotonic aqueous solution (never oily solution) greatly assist suckling infants when instilled before their feeds.

Acute Pharyngitis.

With the possible exception of colds, the physician encounters no other childhood diseases so frequently as acute inflammation of the pharynx and tonsils. Even so, the condition is often missed, because of the peculiar fact that small children complain of abdominal pain rather than of sore throats, and because of the technical difficulties of making an adequate inspection. Again, if the onset of acute pharyngitis is with convulsions, these may be regarded as an illness in themselves and the real nature of the condition may be overlooked.

Formerly pharyngitis was assumed to be always a bacterial infection, usually with group A hæmolytic streptococci, but it now seems that it may exist in two forms. The non-bacterial variety is a fairly mild disease of short duration. The onset is rather gradual with sore throat, hoarseness and cough, at their worst by the third or fourth day. Throat culture reveals no particular organisms, and there is usually no leucocytosis. Streptococcal pharyngitis is generally more acute, but the two varieties cannot with certainty be distinguished on their appearance.

There is always the possibility of diphtheria when one finds membrane on the tonsils and the child has not been immunized. In all doubtful cases a swab should be examined, but if there is reasonable suspicion one should give antitoxin without waiting for the result of the swab examination.

The attempt to treat acute pharyngitis with gargles and throat paints distresses small children and should be abandoned. Aspirin, best suspended in a mixture, undoubtedly gives relief, as does a cough linctus containing codeine. Sulphonamides may not always be necessary, but frequently shorten the illness, and if the fluid consumption is adequate they are quite safe.

Chronic Pharyngitis.

The most important symptoms of chronic pharyngitis are constant clearing of the throat and a persistent irritative cough, worse at night. The cough is often wrongly attributed to chest trouble. Although generally associated with chronic infection of the tonsils, adenoids or sinuses, the disease may occasionally persist or recur after the tonsils and adenoids have been removed. In such cases it is common to see nodules of hypertrophied lymphoid tissue on the posterior pharyngeal wall.

As the treatment of chronic pharyngitis so often involves removal of the tonsils, the indications for this operation must be briefly mentioned. The principal indication is persistent infection, revealing itself by repeated attacks of acute tonsillitis, and perhaps between attacks by such symptoms as listlessness, poor appetite, cough, failure to thrive and pains in the limbs. The tonsils are red, and perhaps examination reveals cheesy material in the crypts and redness of the anterior faucial pillar. Enlarged glands can generally be found at the angles of the jaw. Mere enlargement of the tonsils, unless excessive and causing obstruction in the throat, is not an indication for their removal. Frequent colds do not justify tonsillectomy. Glover, indeed, holds that the frequency of colds is slightly increased in schools with a high tonsillectomy rate.

Radium therapy is of benefit in a proportion of cases of post-operative hypertrophy of lymphoid tissue in the pharynx, accompanied by infection.

Acute Retropharyngeal Abscess.

Suppuration in one of the lymph glands which lie on either side of the mid-line behind the pharynx and in front of the vertebræ produces acute retropharyngeal abscess. This dramatic condition is uncommon and more or less confined to infants and young children.

After an acute throat infection the child becomes worse and seems to find difficulty in swallowing. He refuses drinks and dribbles saliva. His temperature is high and he lies with his head retracted and to one side, with his mouth open. As a rule swollen glands are evident in the neck.

Inspection may not reveal the true condition, as the bulge of the abscess may be out of sight behind the tongue, and in any case much mucus and saliva is present in the mouth. Palpation with the forefinger is essential for diagnosis. The abscess should be opened as soon as it feels soft, as death can follow spontaneous rupture. Evacuation is carried out under vision without anæsthesia, the child being securely held in the head-low position. There is sometimes a surprising amount of pus, and the surgeon must be ready to introduce a sucker the moment his incision is made.

Acute Peritonsillar Abscess (Quinsy).

By way of contrast, acute peritonsillar abscess is rare in infancy and more common in older children. Difficulty in opening the mouth is a characteristic symptom. Inspection reveals an intensely red swelling around the tonsil and an

œdematous uvula displaced to the opposite side of the throat. Exudate may be present on the tonsils. It is important not to confuse this with the severe type of diphtheria with its associated "bull-neck". Such children may have membrane on the tonsils and elsewhere, and extreme bilateral œdema of the fauces as well as of the soft tissues of the neck.

Acute Catarrhal Laryngitis (Croup).

Acute catarrhal laryngitis has been defined as "an acute, self-limited, but usually recurrent, catarrhal inflammation in which the severity of the laryngeal spasm is out of proportion to that of the infection". It is usually encountered during winter in the nervous type of children aged between two and four years. After a preliminary coryza the attack of "croup" occurs rather suddenly at night, with crowing, inspiratory stridor and dyspnœa and much emotional distress. It tends to pass off towards morning, but may be repeated the following night. Although alarming to parent and child, "croup" is not dangerous and the doctor's attitude can be reassuring. Treatment involves the provision of warm moist air, by steam kettle or mechanical humidifier, and the traditional emetic. Phenobarbital (0·5 grain) is a useful adjunct. It is important not to overlook the possibility of laryngeal diphtheria, which is of slower onset and steadily progressive.

Acute Laryngo-tracheo-bronchitis.

The popularity of immunization, of course, is making laryngeal diphtheria uncommon. With its decline, acute laryngo-tracheo-bronchitis has become more generally recognized. This condition, probably of virus origin with secondary bacterial invaders, often occurs in small epidemics. It is characterized by an intense inflammation of the larynx, trachea and bronchi, causing in its early stages laryngeal obstruction from subglottic œdema. At a later stage multiple obstructions develop in the tracheo-bronchial tree by reason of the thick, viscid and crusting exudate which is produced. Tracheotomy relieves the laryngeal obstruction, but for some days afterwards there may be the greatest difficulty in maintaining an airway in the lower part of the trachea and bronchi. To avoid this it is essential to keep the atmosphere saturated with moisture and to facilitate the expulsion of tracheal secretions by suction preceded by instillation of saline. Bronchoscopic suction and removal of plugs may be necessary. Antibacterial drugs help to control the secondary infection and have lowered the mortality rate, which used to be very high.

Acute Bronchitis.

Except as an accompaniment of colds and of measles, acute bronchitis is not a particularly common disease of children. It represents the downward spread of an upper respiratory tract infection. Cough is the chief complaint, at first hard and dry and accompanied by retrosternal pain, but looser after a few days. Rhonchi and coarse râles may be heard all over the chest. There is no great constitutional upset. Bronchitis is dangerous only to weakly infants, in whom a further spread to the lung alveoli is to be feared.

Pneumonia.

Owing to the variability of its clinical pattern, the diagnosis of pneumonia in a sick child often presents difficulties. Sudden illness perhaps arises with high fever, vomiting and stiff neck. Lumbar puncture reveals clear, sterile cerebrospinal fluid under pressure, and the diagnosis remains in doubt until an X-ray examination discloses consolidation at the lung apex. Another child complains of stomach-ache and vomiting, and has a high temperature with abdominal tenderness and guarding of the right rectus. The chest appears clear, and only close observation reveals the hurried respiration, the inverse respiratory rhythm, the flushed cheeks, the slight movement of the *alæ nasi*, the occasional cough and the rather quiet breath sounds at the base of the right lung.

A simple diagnosis of pneumonia is in these days inadequate. One should try to establish whether the disease is of virus or bacterial origin, and, if it is the latter, the nature of the organisms recoverable from the throat swabs or sputum and their sensitivity to the various antibacterial drugs should be determined. One should also decide whether the pneumonia is complicated by, or accompanied by, pulmonary suppuration. This is of more importance than deciding whether the lung involvement is lobar or bronchopneumonic. Pneumococcal pneumonia, for instance, tends to occur in the lobular form during the first year of life and thereafter as lobar pneumonia, but in either case the mode of infection and the treatment are the same.

Virus pneumonia in children has attained prominence in recent years, and in a series of cases reported from Stockholm 23% were of this nature. The illness begins gradually without sudden pain in the side or chill. The principal symptom is a hard, dry cough, often very painful; otherwise the patient's condition is good and unaffected by the high fever. High titres are obtained on cold agglutination tests, maximal between the fifteenth and twentieth days. X-ray pictures reveal hilar thickening with enlarged lymph nodes and patchy bronchopneumonia which spreads or migrates. The leucocyte count tends to be normal. The course is benign and usually uncomplicated, the fever lasting five to seven days when the condition is untreated and less if aureomycin is employed.

Staphylococcal pneumonia is relatively common in infancy and has a special tendency towards necrosis and abscess formation in the consolidated lung. Multiple small abscesses may form. When one of these is situated close to the pleura, perforation may occur, leading to empyema or pyopneumothorax.

Although the most vital part of the treatment of pneumonia consists in giving the appropriate antibacterial drugs, the importance of allowing children adequate rest must not be overlooked. This involves freedom from unnecessary bathing, changing of clothes or other nursing procedures, and from too frequent medical examinations. Sucking at a bottle is hard work for small, sick babies, and feeds should be given by gavage when obvious fatigue is present.

Oxygen can be life-saving and is most effectively given in a tent, a concentration of 40% or more being aimed at. Intranasal catheters are relatively ineffective. A common mistake is to fail to give oxygen soon enough. Dyspnœa and restlessness even without cyanosis are adequate indications. Oxygen reduces the restlessness better than sedatives and is much to be preferred.

Kerosene Pneumonia.

The accidental swallowing of kerosene is frequently accompanied by its aspiration into the lungs, where it proves intensely irritating. (The experimental instillation of kerosene into the tracheas of rabbits regularly produces pneumonia.) Children so affected show a rise in temperature and respiratory rate, but no definite signs in the chest except suppressed breath sounds and a few râles. X-ray diagnosis, based on the finding of patchy bronchopneumonia, is more accurate. Gastric lavage after the swallowing of kerosene should be cautiously performed lest aspiration occur. Indeed, unless the child is examined very early, it is probably better not employed.

Lipoid Pneumonia.

Lipoid pneumonia, first described in 1925, is an important though somewhat rare disease. Commonest in infancy, it may arise from the intranasal instillation of oily drops, or from swallowing difficulties in babies with cleft palate. It can also be produced by forcible attempts to thrust cod liver, castor or mineral oils upon crying children. Not all oils are equally damaging to the lungs, those of animal origin being the worst. Liquid paraffin is chemically inert, but acts as a foreign body. The symptoms of lipoid pneumonia appear insidiously after a varying period of cough. X-ray films reveal dense hilar shadows extending into the lung fields especially towards the bases. The prognosis depends upon the degree of pulmonary damage at the time when the disease is discovered; it is often fatal, and recovery is always slow.

Sinusitis and Bronchitis.

Although the antra and the ethmoid sinuses are present at birth, sinusitis is essentially a disease of later childhood. Acute infection, other than that accompanying a cold, is not common and will not be further discussed. Chronic sinusitis occurs frequently, producing such vague symptoms as malaise, headaches, poor concentration, anorexia and attacks of sneezing. Post-nasal discharge, if adenoid infection can be excluded, is almost diagnostic.

The frequent association of sinus infection with disease of the bronchial tree has led to the use of the term "bronchosinusitis". Opinions differ as to whether repeated aspiration of infective material from the upper air passages into the bronchi, or coughing of mucopus into the nasopharynx, is the more important mechanism. Often the child's bronchitis and sinusitis become manifest simultaneously, and both usually clear together. Probably the essential factor is one affecting the whole respiratory tract, such as malnutrition, allergy or perhaps an inherited ineffectiveness of the cilia. There is certainly a familial tendency.

The importance of good ciliary action in maintaining the sterility of the respiratory tract can hardly be overestimated. By their constant action the cilia move a cover-

ing film of mucus steadily towards the exterior at an average speed of 2·0 centimetres per minute in the nose and 0·25 centimetre per minute in the bronchi. No treatment should be used which interferes with this action. Accumulated secretions, too heavy to be moved by the cilia, should be evacuated according to their locality by posture, suction or drainage.

The child with a persistent cough, the result of chronic infection of his chest and sinuses, is apt to prove a serious problem to his doctor. The cough is usually worse at night and in the wintertime, often clearing in the warmer weather. Physical signs are limited to scattered rhonchi and coarse râles, most plentiful in the lower lobes. Bronchiectasis can be eliminated only by a bronchogram.

Treatment must have regard to the child's general health and nutrition, the neutralization of allergies and the management of the associated sinusitis. Long courses of treatment with sulphamerazine have proved helpful. Transfer to a warm, dry climate may be the only way of curing a persistent infection.

Bronchiectasis.

One encounters many children with chronic bronchitis or "bronchosinusitis" who are in the process of developing bronchiectasis. They suffer from prolonged loose cough, interspersed with upper respiratory tract infections, and their bronchograms show a mild degree of cylindrical dilatation of some of the lower lobe bronchi. Some of these children eventually recover, but a few progress slowly to more definite bronchiectasis. The essential factor in this downward progress is bronchial obstruction, followed by atelectasis. Infection is a secondary and less important factor.

Bronchiectasis is not at all an uncommon disease, and in 65% of cases it develops within the first two decades of life. It is so unpleasant in its symptoms, so dangerous in its prognosis and (despite some surgical triumphs) so unsatisfactory to treat that every possible effort should be devoted towards its prevention.

Harwood, in a recent article in this journal, described as "pre-bronchiectatic" any child who had had whooping-cough, measles, bronchopneumonia, pink disease or pneumonia, and who had been left with a cough, not always productive, for eight to ten weeks after the infection. This is particularly so when nasal discharge is also present and when the patient is allergic or has an allergic family history. Children showing such symptoms in spite of careful treatment of the initial disease and adequate convalescence need active and special treatment if the development of true bronchiectasis is to be avoided. If inhalations to loosen secretions, postural drainage and encouragement of coughing are unsuccessful, bronchoscopic examination must be undertaken, and the thick, tenacious secretions must be removed by suction. This takes the load off the clogged cilia, establishes an adequate airway to the alveoli and reestablishes normal physiological upward drainage by ciliary wafting.

The surgical treatment of established bronchiectasis will not be considered here.

Fibrocystic Disease.

No account of the respiratory tract infections of children would be complete without mention of the pulmonary manifestations of cystic fibrosis of the pancreas. They are often the first symptoms. Persistent respiratory tract infection beginning within the first few weeks of life is always suggestive. Physical signs of obstruction of various parts of the bronchial tree are often present, and a generalized expiratory type of dyspnœa due to widespread bronchiolar obstruction is common. The severe cough results from the difficulty in expulsion of the thick, tenacious mucus produced in the trachea and bronchi. Ciliary movement is impaired, secondary bacterial invasion of the lung being permitted, generally with the *Staphylococcus aureus*. The X-ray film reveals greatly accentuated hilar markings with the bronchi standing out prominently. Small foci of consolidation are seen about the bronchi, with larger areas farther out in the lung parenchyma. In extensive disease areas of emphysema and atelectasis are apparent. Bronchoscopic examination reveals hyperæmic bronchial mucosa, the lumen being obscured by extremely viscid mucus or mucopus. In many infants the respiratory symptoms, especially the pertussis-like cough, are so pronounced that they overshadow the gastro-intestinal symptoms, and the exact nature of the illness is obscured. About one-half of the infants with this disorder die of pulmonary infection before the sixth month of life.

FELIX ARDEN,
Brisbane.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on December 6, 1951, at the Saint George Hospital, Kogarah. The meeting took the form of a number of clinical demonstrations by the members of the honorary medical and surgical staffs of the hospital.

Malignant Hypertension Treated with Hexamethonium Bromide.

DR. J. S. BOXALL and DR. K. C. JACKSON showed an unmarried female patient, aged twenty-two years, who complained of headaches, from which she had suffered for three years, and which were growing more severe, and of becoming breathless easily. She had no urinary symptoms. On October 8, 1951, Dr. R. Hertzberg, the honorary ophthalmologist, examined her eyes and reported that the visual acuity was 6/6; the disks were blurred, and there were patches of exudate and a flame-shaped hæmorrhage in the fundus of the left eye. The patient's blood pressure was 220 millimetres of mercury, systolic, and 160 millimetres, diastolic. The urine contained albumin. A provisional diagnosis of malignant hypertension was made. On October 10 a blood count showed that the erythrocytes numbered 4,700,000 per cubic millimetre and the hæmoglobin value was 101%. A urea concentration test showed that the concentration was 53% of normal. Albumin was present in all specimens of urine. The fasting blood urea content was 36 milligrammes *per centum*. An electrocardiogram revealed no abnormality. Radiological examination of the lungs revealed normal appearances, and no abnormality was detected by excretion pyelography.

On October 30, treatment with "Vegolysen" (hexamethonium bromide) was begun, the dose being 250 milligrammes three times a day before meals; one-quarter of a grain of phenobarbital was given three times a day after meals. On November 6 the patient's blood pressure was 190 millimetres of mercury, systolic, and 150 millimetres, diastolic, and she still had some headache. The dose of "Vegolysen" was increased to 500 milligrammes three times a day before meals; this resulted in sickness, relieved by the patient's lying down. The blood pressure dropped to 128 millimetres of mercury, systolic, and 108 millimetres, diastolic. The dose of "Vegolysen" reverted to 250 milligrammes three times a day before food.

On November 26 Dr. Hertzberg examined the patient's eyes again, and reported that he could find no abnormality in the fundi, no hæmorrhages and no exudate. On November 27 the blood pressure was 180 millimetres of mercury, systolic, and 140 millimetres, diastolic, and the patient's headaches were much better. The urine contained a heavy cloud of albumin.

It was pointed out that the effect of hexamethonium bromide was fivefold: (i) suppression of gastric motor and secretory activity, (ii) production of hypotension, (iii) peripheral vasodilatation, (iv) paralysis of visual accommodation and (v) reduction of bowel tonus.

Spontaneous Hypothyroidism.

Dr. Boxall and Dr. Jackson then showed a married woman, aged fifty-seven years, who complained that she tired easily, that she had been overweight for twenty-seven years, that she was sleepy and had a dry skin, that she felt both the heat and the cold, and that she suffered from headache. The patient had three children, of whom the youngest was aged thirty-one years. She had undergone an appendicectomy twenty years earlier, but had had no severe illnesses. Her menstrual periods had ceased eight years earlier.

On examination of the patient on November 13, 1951, she was found to weigh 13 stone 11 pounds, and her skin was dry and waxy. Non-pitting œdema was present. Her pulse rate was 80 per minute, and the pulse was slightly irregular; the heart sounds were faint. Her blood pressure was 160 millimetres of mercury, systolic, and 110 millimetres, diastolic. An electrocardiographic examination revealed auricular fibrillation, myocardial degeneration, flattened *T* waves and low voltage. X-ray examination of the chest revealed that the heart was enlarged, chiefly towards the left. A blood count gave the following findings: the erythrocytes numbered 4,200,000 per cubic millimetre, the hæmoglobin value was 78% and the leucocytes numbered 7900 per cubic millimetre. The basal metabolic rate was −25%.

The plasma cholesterol content was 43 milligrammes per 100 millilitres (normal, 150 to 250 milligrammes). X-ray examination of the pituitary region revealed no abnormality.

The patient was treated with thyroid (0·5 grain three times a day to begin with), "Digoxin" (0·25 milligramme three times a day), 0·5 grain of phenobarbital at night, and "Polyhæmin".

Possible Lymphadenoma.

Dr. Boxall and Dr. Jackson finally showed a male patient, aged forty-two years, who had had enlarged glands for one year and complained of loss of energy.

On examination of the patient, enlarged rubbery glands were present in the neck, groins and axillæ, and the spleen was enlarged. A blood count gave the following information: the erythrocytes numbered 4,900,000 per cubic millimetre, the hæmoglobin value was 94% and the colour index was 1·0; the leucocytes numbered 5800 per cubic millimetre, 65% being neutrophile cells, 10% lymphocytes, 10% monocytes and 15% eosinophile cells. The result of the Wassermann test was not available at the time of the meeting. X-ray examination of the chest revealed no abnormality and no mediastinal enlargement. The Paul-Bunnell test produced a negative result. A biopsy was performed and the tissue was examined by Dr. A. E. Gatenby, pathologist to the hospital, who reported the result as "? lymphadenoma". The diagnosis was thought to be (i) mononucleosis, (ii) syphilis or (iii) lymphoblastoma. The patient was to be given X-ray therapy if the pathological diagnosis was confirmed.

The comment was made that groups of glands became enlarged in the following order: cervical, axillary, inguinal, mediastinal, mesenteric and retroperitoneal. Splenomegaly was present in 60% of cases. Investigation of the blood picture sometimes revealed lymphocytosis with an increase in the number of monocytes; later eosinophilia developed, the proportion of eosinophile cells rising to 60% or even 90%, and later still anæmia—simple, hypochromic, macrocytic or hæmolytic. Histopathological examination of tissue revealed lymphoid hyperplasia, endothelial cells, leucocytes, and eosinophile cells in the sinuses, and Dorothy Reed giant cells.

Guillain-Barré Syndrome.

DR. J. C. ENGLISH and DR. N. MANION first showed a married woman, aged fifty years, who on March 1, 1950, had noticed pain between her shoulders. Next day she had noticed tingling in her feet and pain in the lower lumbar region of the spine. She had a cold in the head next day, but was able to move around slowly. Weakness developed in both her legs during the next week, and intermittently in her hands. A few days later her speech became strange and her tongue weak. When she was first medically examined on March 8, she had unilateral facial palsy, and in view of her history and the absence of tendon reflexes in the legs she was admitted to a hospital as possibly suffering from poliomyelitis.

On March 23 a microscopic and biochemical examination of the cerebro-spinal fluid was made. The red cells numbered 12 per cubic millimetre; no leucocytes were present. The protein content was 60 milligrammes per 100 millilitres, and the chloride content was 740 milligrammes per 100 millilitres. The patient was later discharged from that hospital, and was admitted to the Saint George Hospital on May 4, 1950.

On examination of the patient the following abnormalities were present: (i) flaccid quadriplegia, complete in the lower limbs, almost so in the upper limbs; (ii) bilateral facial paralysis; (iii) pronounced hyperæsthesia and hyperalgesia of the lower limbs; (iv) retention of urine; (v) diminished respiratory excursion with râles at the bases of both lungs. She was clear mentally and gave an orderly history. On May 5 a microscopic and cultural examination of the urine was undertaken; no abnormal constituents were seen in a wet film, and coliform organisms were recovered in culture. On June 8 a microscopic and biochemical examination of the cerebro-spinal fluid revealed no cells; the chloride content was 740 milligrammes per 100 millilitres, the protein content 180 milligrammes per 100 millilitres and the sugar content 55 milligrammes per 100 millilitres. Gram staining revealed no organisms. No tubercle bacilli were revealed by Ziehl-Neelsen staining.

During the next six or seven weeks the patient's progress was marked by febrile episodes with chest signs, for which penicillin was used, by occasional bouts of dyspnœa with cyanosis requiring oxygen, and by gradual improvement in her bladder function, respiration and muscle power.

On July 4 a microscopic and biochemical examination of the cerebro-spinal fluid gave the following results. The cells present consisted of two lymphocytes and one polymorphonuclear leucocyte per cubic millimetre; the chloride content was 740 milligrammes per 100 millilitres, the protein content was 96·7 milligrammes per 100 millilitres and the amount of sugar present was within normal limits.

On September 30 the patient was discharged from hospital; she was able to walk with sticks, but toe-raising springs were needed for her feet. She was soon able to drive a motor-car, and finally discarded the foot springs. Her progress was steady thereafter. She was able to do full housework. She had sustained a fracture of the fibula eight weeks prior to the meeting, and X-ray examination showed that skeletal decalcification was still present. Healing was rapid.

The comment was made that the patient was shown to illustrate the severity of the condition, the excellence of the prognosis for recovery of function if death was averted, and finally the long duration of the bony change even when full activity was present, and the possibility of fracture in such cases even after recovery appeared full.

Refractory Anæmia.

Dr. English and Dr. Manion next showed a female patient, aged fifty-one years, who had been referred for investigation of refractory anæmia. Several tests of the urine had failed to reveal albumin or casts. On December 8, 1949, a full blood count had given the following results: the erythrocytes numbered 2,500,000 per cubic millimetre, the hæmoglobin value was 65% (9·0 grammes *per centum*), and the colour index was 1·2; slight anisocytosis, moderate macrocytosis and slight poikilocytosis were present. The leucocytes numbered 6500 per cubic millimetre, and the different types of cells were present in normal proportions. The pathologist reported the presence of macrocytic anæmia of moderate degree; the blood film appearances were not characteristic of pernicious anæmia, and it was suggested that other causes of macrocytic anæmia should be considered. The pathologist thought that a fractional test meal examination and a Van den Bergh test might be helpful in elucidating the diagnosis.

On February 2, 1950, a fractional test meal examination showed that no free acid was present. The direct Van den Bergh test produced a negative result. The total serum protein content was 7·0 grammes *per centum*, the thymol turbidity was two units, and the serum alkaline phosphatase content was 8·2 King-Armstrong units.

On March 15, 1950, the patient was admitted to hospital for biopsy of the bone marrow. She gave a history of vague ill health for years. She had suffered from weakness and breathlessness and swelling of the ankles for three years, but had no urinary symptoms. The medical practitioner who had referred her stated that she was suffering from anæmia of slightly macrocytic type unresponsive to liver injections.

On examination of the patient, she was seen to be pale; the liver and spleen were not palpable, and no abnormality was detected in her chest. Her pulse rate was 80 per minute, and the pulse was regular in time and amplitude. Her blood pressure was 170 millimetres of mercury, systolic, and 100 millimetres, diastolic; the heart sounds were normal. The urine was acid and clear. A specimen of bone marrow was taken for examination from the left iliac crest, by Dr. Gatenby; only a minute quantity was obtained. A differential nucleated cell count gave the following figures (the normal figures given are according to Piney): (i) Neutrophile cells: myelocytes 12% (normal, 30% to 35%), metamyelocytes 9% (normal, 10% to 15%), polymorphonuclear leucocytes 25% (normal, 24% to 30%). (ii) Eosinophile cells: myelocytes 5% (normal, 1% to 2%), mature myelocytes 3% (normal, 0·5% to 1%), premyelocytes 7% (normal, 1% to 2%), lymphocytes 28% (normal, 14% to 21%). (iii) Monocytes 2%. (iv) Megaloblasts, nil (normal, 2% to 3%); erythroblasts 3% (normal, 1% to 2%); normoblasts 6% (normal, 15% to 20%). Numerous unclassifiable cells were present. Dr. Gatenby reported that the appearances of the marrow and the blood count suggested anæmia due to some hypoplasia of the bone marrow; but the hypoplasia did not appear to be severe, as there was evidence of regeneration both in the marrow and in the blood films. Dr. Gatenby considered that iron therapy was still indicated, and that a careful search should be made for chronic hæmorrhage or any likely source of hæmotoxins, such as sepsis, nephritis *et cetera*.

On September 13 the result of a urea clearance test was 10% of normal. On November 9 a blood count showed that

the erythrocytes numbered 2,900,000 per cubic millimetre, the hæmoglobin value was 70% (9·8 grammes *per centum*) and the colour index was 1·1. No significant changes were seen in a stained film. Excretion pyelography was carried out, and practically no dye had been excreted by either kidney up to thirty-five minutes after the injection. On November 14 the urine was examined by microscopic and biochemical methods and by culture. In a wet film a few pus cells and occasional red cells were present; no casts were seen. A faint cloud of albumin was present. No organisms were recovered on attempted culture.

On January 25, 1951, a blood count gave the following information: the erythrocytes numbered 2,500,000 per cubic millimetre, the hæmoglobin value was 57% (7·8 grammes *per centum*) and the colour index was 1·0. On January 30 the patient was admitted to hospital for cystoscopic examination and bilateral retrograde pyelography. She gave a history of lassitude and pallor of two years' duration, of dyspnœa on exertion of three years' duration, and of swelling of the ankles of four or five years' duration. She had been in good health about five years earlier. Three years prior to the meeting she had had to give up work because she became breathless on walking upstairs at the railway station. Prior to that she had noticed almost constant œdema of the ankles Over the past two years she had suffered from increasing lassitude, tiredness and pallor. She had undergone an appendicectomy ten years previously. She had no history of hæmaturia, but she had suffered from pyelitis six or seven months prior to the meeting. The patient on being questioned said that she became breathless on exertion, but had no nocturnal dyspnœa; she felt a knife-like retrosternal pain on exertion. No enlarged glands were present. The patient had had varicose veins for twenty years.

On examination, the patient was seen to be pale. The pulse rate was 80 per minute, and the pulse was regular in time and amplitude. The blood pressure was 180 millimetres of mercury, systolic, and 100 millimetres, diastolic. The apex beat was in the fifth left intercostal space, in the anterior axillary line. The heart sounds were normal and no abnormality was detected in the chest. The spleen was not palpable; the liver edge was just palpable and slightly tender. Tenderness was present in both loins. The kidneys were not palpable. The pupils reacted to light and accommodation. No other abnormalities were present. The urine was acid and clear.

On January 31 a cystoscopic examination and bilateral retrograde pyelography were carried out. Both renal pelves were seen to be dilated, and their lower borders were horizontal, although on the left side the border sloped slightly upwards and there seemed to be some obstruction at the pelvi-ureteric junctions. The major calyces were distended and widened, and only a small amount of renal parenchyma was seen on both sides. The picture was thought to be compatible with that of chronic nephritis, associated with bilateral aberrant vessels. Both kidneys appeared small. The patient was discharged from hospital on February 1, 1951.

On February 8 it was thought that no urological procedure was indicated. A reticulocyte count was made, the resulting figure being 2%. Treatment with intravenous injections of "Ferrivenin" twice a week was instituted. On March 1 the reticulocyte count was 0·5% and the hæmoglobin value was 69% (9·6 grammes *per centum*); "Ferrivenin" treatment was suspended. On March 8 it was decided to give the patient eight millilitres of "Campolon" intramuscularly, and to make a reticulocyte count in one week; the figure obtained was 1·0%, and "Campolon" treatment was suspended. On March 9 the fasting blood urea content was 160 milligrammes *per centum*. On March 22 treatment with "Pentavite" was instituted. On May 18 the hæmoglobin value was 75% (10·3 grammes *per centum*), and on May 24 the patient was fairly well, but had dyspnœa of effort; her blood pressure was 190 millimetres of mercury, systolic, and 100 millimetres, diastolic. On August 2 the hæmoglobin value was 92% (12·8 grammes *per centum*), the fasting blood urea content was 66 milligrammes *per centum* and the blood uric acid content was 6·0 milligrammes *per centum*. On October 11 the urine was clear; the blood pressure was 190 millimetres of mercury, systolic, and 100 millimetres of mercury, diastolic. On November 9 the hæmoglobin value was 75% (10·4 grammes *per centum*) and the fasting blood urea content was 100 milligrammes *per centum*. By November 15 the patient was feeling well; she had morning headache, and passed urine often during the day and three or four times during the night. Her tongue was clear and her breath was normal. Her blood pressure was 172 millimetres of mercury, systolic, and 100 millimetres, diastolic, the optic fundi were normal and the urine contained a cloud of albumin. On December 1 microscopic examination of the urine revealed many pus cells; no organisms were grown on attempted culture. The blood uric acid content was 8·0 milligrammes *per centum*, and the fasting blood urea content was 100 milligrammes *per centum*. A full blood count gave the following information: the erythrocytes numbered 4,000,000 per cubic millimetre, the hæmoglobin value was 93% (12·8 grammes *per centum*), the colour index was 1·05, and the hæmatocrit reading was 38%. The mean corpuscular volume was 95 cubic μ (normal, 75 to 95 cubic μ), the mean corpuscular hæmoglobin was 32 microgrammes (normal, 26 to 31 microgrammes), and the mean corpuscular hæmoglobin concentration was 35% (normal, 33% to 39%). Examination of a stained film revealed a variable hæmoglobin content, slight anisocytosis and polychromasia, and occasional macrocytes and microcytes. The leucocytes numbered 4500 per cubic millimetre, and the distribution was normal.

Dystrophia Myotonica.

DR. J. V. LATHAM AND DR. B. HANEMAN showed a male patient, aged fifty years, showing the classical features and characteristic facies of *dystrophia myotonica*. Ever since he was a boy he had had difficulty and delay in releasing from his hand objects he had gripped. For some years he had had his own heavy, "floppy" tread. In 1938, while at Victoria Barracks, he fell and hurt his ankle. Immediately afterwards he took part in some drill and went home feeling warm and well. Nearly an hour later, on reaching his home station, he found great difficulty in walking and in general muscular movement, so that a walk which normally lasted nine minutes actually needed twenty-five minutes. Since then he had fallen more and more, and had become weaker, till now he could rise from his chair only with difficulty. Four years prior to the meeting he fell and broke two ribs. Since then he had noticed a weak productive cough. He had no children and no libido. His mother at the age of seventy years had a cataract, but no relevant family history.

On examination of the patient, pronounced wasting of the facial muscles and sternomastoids was present, and also moderate wasting of the arms and legs and a sagging abdominal wall. Frontal baldness was obvious. Testicular atrophy was present. The deep reflexes were absent, but the plantar response was normal. There was no sensory loss. The chest expansion was one inch, and the patient had a "juicy" cough and râles at the base and mid-zone of the right lung.

On May 17, 1951, an X-ray examination of the chest revealed that the right dome of the diaphragm was very high; it was probably partially paralysed. There was considerable increase in lung markings at the base of the right lung, probably chiefly the result of poor aeration. The lung fields appeared to be clear otherwise.

The comment was made that taken together, the peculiar myotonia (well seen when the thenar eminence was struck) and the characteristic dystrophy and its distribution made the diagnosis certain. The only other condition showing myotonia was *myotonia congenita* (Thompsen's disease). Together with the still rarer *paramyotonia congenita*, those three conditions were probably all related. The myotonia was due to a change in the muscle fibre, which was extremely sensitive to mechanical stimulation. Even response to a single motor nerve shock was a long tetanic contraction instead of the normal short twitch. In treatment quinine was of value, and exercise helped.

Familial Hæmorrhagic Telangiectasia (Rendu-Osler-Weber's Syndrome).

Dr. Latham and Dr. Haneman then showed a postman, aged fifty years, who in July, 1951, had complained of severe indigestion, present intermittently for six weeks. Very soon after almost every meal he experienced severe mid-epigastric pain, together with a strong sense of mid-sternal blockage on swallowing food. Antacid powders gave him a limited amount of relief. He had no special food intolerance. At one time even a drink of water caused pain. Each morning he vomited "bile", and simultaneously his nose bled. He had lost no weight and had no night pain. On hurrying, too, he developed constricting chest pain, radiating from navel to neck, which caused him to halt; the pain did not radiate down the arm. In 1947 and 1949 the patient had been admitted to the hospital because of hæmatemesis and melæna, without any obvious preceding ulcer symptomatology. On both occasions X-ray study with opaque media failed to reveal a cause. He responded well to conservative treatment. He was hypertensive. At the time of the meeting he smoked two ounces of tobacco per week. His mother

suffered from hæmatemesis. His children (some present at the meeting) had red spots similar to his own.

On examination of the patient, the text-book picture of nævi on the face, nose, lip, tongue and palate was present. There was no epigastric tenderness, and neither the spleen nor the liver was enlarged. His blood pressure was 170 millimetres of mercury, systolic, and 120 millimetres, diastolic. A few fine post-tussive basal crepitations were present. An electrocardiogram prepared on August 9, 1951, showed an abnormal record; the rate was 80 per minute, the rhythm was regular, the *P-R* interval was 0·21 second, and the *QRS* complex was of low voltage and slurred. The tracing suggested myocardial disease. Examination by means of a barium meal on August 24 revealed some tendency to spasm at the lower end of the œsophagus, and there was a small herniation of the stomach through the œsophageal opening of the diaphragm. The stomach was normal. The duodenal cap was irritable and somewhat tender to local pressure. No ulcer crater could be detected there now, but it had possibly been the site of recent ulceration. On July 19 a blood count gave the following information: the erythrocytes numbered 5,500,000 per cubic millimetre, the hæmoglobin value was 16·0 grammes per 100 millilitres and the platelets numbered 300,000 per cubic millimetre. The bleeding time was one and a half minutes and the coagulation time was three and a half minutes at 37° C.

At the time of the meeting the patient was doing light work, and taking trinitrin, "Prænitron" and magnesium trisilicate. Both his dyspepsia and his angina were much less. Each morning he vomited bile, and mostly his nose bled also.

It was pointed out that without endoscopic examination there was no proof that his alimentary hæmorrhages came from gastric nævi, rather than from a duodenal or œsophageal ulcer. However, the diagnosis of familial hæmorrhagic telangiestasia seemed secure. The condition had the following characteristics: it was familial or hereditary (Mendelian dominant); it affected the sexes equally; nævi usually became apparent after puberty; the skin and mucous membranes were involved—the skin affected was chiefly that of the face, nose, mouth and sometimes fingers; and the mucosa—that of the mouth, the pharynx, and the alimentary, respiratory and renal tracts. Severe hæmorrhage might occur from any site. Epistaxis was the commonest symptom.

(To be continued.)

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

GOVERNOR MACQUARIE TO EARL BATHURST.[1]

[Historical Records of Australia.]

15 May, 1818.

My Lord,

I should be doing violence to my own feelings, as well as great injustice to the merits and claims of Mr Wentworth, if I did not embrace the present opportunity of bearing testimony to the indefatigable zeal, vigilance, activity, honor, and integrity uniformly manifested by him in the due execution and faithful discharge of his various important Public Duties during the period of my administration of this colony, now upwards of eight years. I have ever found Mr Wentworth honest, honorable, just, and humane in the execution of his various functions, and at all times ready and willing to promote the public Service by every means in his power. He has been extremely active, zealous, and useful in his magisterial Capacity, devoting almost the whole of his time to the Police Department which is a most arduous and troublesome duty: but which has been very ably conducted under his superintendence. In succession to Mr Wentworth as Principal Surgeon in the Medical Establishment of this Territory I beg most respectfully to recommend Mr Assistant Surgeon William Redfern to be appointed *Principal Surgeon*, as in every respect perfectly competent, and well qualified for executing the Duties of that important Office, being a man of very eminent talents, an excellent scholar, and possessing universal knowledge. Mr Redfern is at present only Second Assistant on the Medical Establishment, Mr James Mileham being the First and Senior Assistant. But this Gentleman, tho' a very worthy good man, is very defective in medical knowledge: he is old and very much affected in his eyesight, which render him incompetent for the active and important Duties of Principal Surgeon. These are my sole motives for passing over Mr Mileham and recommending Mr Redfern, the next Officer in Succession to him, and these reasons I trust will have their due weight with your Lordship.

I have, &c.,

L. Macquarie.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

THE NOTIFICATION OF TUBERCULOSIS IN NEW SOUTH WALES.

Sir: The letters of my esteemed colleague on this subject would perhaps be more convincing if they advanced any valid reason why one notifiable disease should be differentiated from all the rest in respect of the notification fee. The latter is purely nominal, and was apparently designed to cover costs of postage or, in some diseases, of notification by telegraph or telephone. After all, abuse, though often self-revealing, convinces nobody.

It may be that the advisory body referred to has found such a reason.

The matter is not quite so trivial as it may seem. Notification is a necessary part of the machinery for effective control of infectious diseases. Notwithstanding that notification is compulsory, the goodwill and cooperation of all sections of the profession are the essential factors. Differentiation which favours one section, however small, is surely to be deprecated.

Yours, etc.,

H. Wallace.

Killara,
New South Wales,
February 12, 1952.

EPIDEMIC HÆMORRHAGIC FEVER OR RYUKOSEI SHUKKETSU NETSU.

Sir: A mistake was made in the figures given in my article in the journal of December 15, 1951. There were 200 cases till the end of September, not October. The total till the end of December equals 894, November being the peak month with 374. There have been very few cases since mid-December and it appears that the disease may have a seasonal incidence and has now run its course. With the increase in the number of cases for the November and December period, approximately 500, there was a decrease in the mortality, which fell to 3%, bringing the over-all mortality to about 5%.

Some further complications have been noted: anuria superseding oliguria, bladder paralysis, a shock phase in which the systolic blood pressure may fall as low as 50 millimetres of mercury, localized Jacksonian fits affecting one limb.

The predominant pathological feature is a paralysis and dilatation of the capillaries affecting all organs in various degrees followed by hæmorrhage and pericapillary œdema.

As mentioned before, the kidneys are always affected. The lungs are involved in all cases. The liver is usually swollen and shows subcapsular hæmorrhages, the spleen is often slightly enlarged and shows the same vascular changes.

The brain shows petechial hæmorrhages in the cortex, and the pituitary gland, chiefly the anterior lobe, is greatly enlarged and hæmorrhagic and in some cases resembles a hæmatoma. The gastro-intestinal tract is markedly hæmorrhagic, and in those cases showing intestinal hæmorrhage the whole tract is a purplish-red colour.

The adrenal gland is hyperæmic, and hæmorrhages occur at the boundary between the cortex and medulla.

The thyroid gland is hyperæmic.

The lymph nodes show hyperplasia of the reticulo-endothelial system and the characteristic disturbances of the vascular system.

With regard to treatment, as time went on less fluid was given to patients who were oliguric or anuric, and severe cases were kept dehydrated until kidney function returned, blood transfusion being reserved for those whose blood pressure fell to any great extent.

Although the electrolytic balance was disturbed, this treatment by dehydration appeared to have a beneficial effect.

I wish to thank Air Commodore E. A. Daley, C.B.E., F.R.A.C.P., K.H.P., Director-General of Medical Services, Royal Australian Air Force, for permission to publish this letter.

Yours, etc.,

N. M. KATER,
Wing Commander, Squadron Medical Officer, 77 (I/F) Squadron.
Royal Australian Air Force,
Korea.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

PROGRAMME FOR APRIL, 1952.

Demonstration on Angiocardiography.

THE Melbourne Permanent Post-Graduate Committee has arranged with Dr. Norbert Klein, of Auckland, New Zealand, for the showing of two films on angiocardiography. The first is a 16-millimetre motion picture entitled "Angiocardiocinematography of the Normal Heart and of Some Congenital Malformations of the Heart". This film originates from Professor Janker (Bonn) and was shown at the last International Congress of Radiology in London, where it was an outstanding success. The second is a 35-millimetre film strip of some of Dr. Norbert Klein's own cases and is entitled "Diagnostic Value of Angiocardiography in Acquired Cardiac and Extrocardiac Conditions".

These films are being shown through the courtesy of Dr. Norbert Klein at 8.15 p.m. on Tuesday, April 22, in the Medical Society Hall, 426 Albert Street, East Melbourne. No charge will be made for admission to this demonstration.

Country Courses.

Sale.

A post-graduate week-end will be held at Sale on April 19 and 20. The programme is as follows: Dr. Charles Sutherland, "Asthma and Allied Diseases"; Dr. John Colebatch, "Infectious Diarrhœa in Infancy and Childhood"; Dr. N. De Garis, "Toxæmias of Pregnancy"; Dr. John Bolton, "Recent Advances in the Management of the Macrocytic Anæmias and of Leuchæmia". The fee for this course is £2 2s., or 10s. 6d. per demonstration, and enrolments should be made with Dr. D. I. Fitzpatrick, 52 Cunningham Street, Sale. Telephone: 174.

Ballarat.

A post-graduate lecture will be delivered at Ballarat on April 26 at 8 p.m. by Dr. E. Drevermann on "Modern Methods of Resuscitation". Enrolments should be made with Dr. J. P. L. Griffiths, Secretary of the Ballarat Subdivision of the British Medical Association, 29 Errard Street North, Ballarat. Telephone: 350. The fee will be 10s. 6d.

Flinders Naval Depot.

At Flinders Naval Depot on Wednesday, April 9, at 2.30 p.m., Dr. B. Keon-Cohen will lecture on "Low Back Pain". This is by arrangement with the Royal Australian Navy.

Classes Suitable for M.D. II and M.R.A.C.P. Candidates.

The pædiatrics course, under the direction of Dr. M. L. Powell, which commenced in March, will continue on April 1 and 4 at 2 p.m.

The thoracic diseases course, under the direction of Dr. Clive Fitts, will be held at 2 p.m. on April 18, 22 and 29 and May 2, 6 and 9.

Classes for Part I of Higher Degrees and Diplomas.

Classes in physiology, anatomy, pathology and physics which commenced earlier in the year will be continued. Details may be obtained from the Post-Graduate Committee.

The Royal Australasian College of Physicians.

AT a special meeting of The Royal Australasian College of Physicians held in Sydney on February 15, 1952, the following resolution was passed. The resolution was subsequently submitted to His Excellency the Governor-General with the request that it be transmitted to Her Majesty the Queen.

The President and Council of The Royal Australasian College of Physicians, assembled in Sydney on 15 February, 1952, express their profound sorrow at the death of His Majesty King George VI and offer to the Queen, the Queen Mother, Queen Mary and other members of the Royal Family the sympathy of all the Fellows and Members of the College. They note with deep pride that this Royal College at its inauguration in 1938 received a message of goodwill from His Majesty.

The College also tenders through its President and Council the fealty of its Fellows and Members to Her Majesty Queen Elizabeth now gloriously reigning and assures her of their loyalty and devotion.

Congresses.

FIRST INTERNATIONAL CONGRESS OF NEUROPATHOLOGY.

THE first International Congress of Neuropathology is to be held at Rome commencing on September 8, 1952. National committees have been formed in 22 countries. The provisional programme is as follows: first day, histopathology of demyelinating diseases; second day, histopathology of vascular diseases; third day, histopathology of schizophrenia; fourth day, histopathology of mental deficiencies; fifth day, histopathology of senility; sixth day, free forum. Membership fee of $15.00 should be forwarded to the chairman of the national committee for Australia and New Zealand, Professor Keith Inglis, Department of Pathology, University of Sydney, Sydney.

DEUTSCHEN GESELLSCHAFT FÜR GYNÄKOLOGIE.

THE twenty-ninth session of the *Deutschen Gesellschaft für Gynäkologie* will be held at Munich from October 7 to 11, 1952. It is thought that the congress may be of interest to readers of this journal. Further information including the programme may be obtained from Professor Dr. W. Rech, Maistrasse 11, München 15 (Germany).

Obituary.

CHARLES ERNEST CAMERON WILSON.

WE are indebted to Professor J. B. Cleland for the following account of the late Dr. Charles Ernest Cameron Wilson.

Charles Ernest Cameron Wilson, who died at Fullarton, Adelaide, on December 20, 1951, at the age of seventy-six years, was born at Kensington, South Australia, on September 27, 1875. All his four grandparents were "pioneers" of 1838-1839. His paternal grandfather was Thomas Wilson, who arrived in the Province in the *Duke of Roxburgh* in 1838, became a partner in the firm of Smart and Wilson, solicitors, was the second mayor of Adelaide (1842-1843), and in 1841 was appointed Clerk of Appeals. Thomas Wilson traced his descent from the Protector Cromwell. He died in 1863. His second son, Charles Algernon Wilson, father of Ernest, was Registrar of Probates and the first clerk to the Supreme Court, one of the earliest members of the Adelaide Philosophical Society (the forerunner of the Royal Society of South Australia) and an entomologist of considerable attainments, who, under the name of "Naturæ Amator", contributed articles on natural history to the Press of the day; he came out with his parents at the age of twenty years and died in 1884. There must be few families

in which a period of one hundred and thirty-three years has elapsed between the birth of the father (Algernon) and the death of the son (Ernest). Ernest Wilson's mother was Mathilda King, whose brother was one of the nine who accompanied the explorer J. McDouall Stuart across the continent. The Reverend Theodore Percival Wilson, who came out in 1847 with Bishop Short and became the first headmaster of Saint Peter's College, was his uncle. The famous naturalist, Alfred Russell Wallace, author of "The Malay Archipelago", was a cousin and school-mate of his father, and Ernest stayed with him when he visited England soon after graduation.

Ernest commenced his medical studies in Adelaide in 1894, but, owing to the notorious Adelaide Hospital trouble, after passing his third year he had to complete the course in Melbourne, going to Trinity College and graduating in 1899. After holding various hospital appointments in Melbourne and England, he was in practice at Wallaroo for nine years and at Kadina for fifteen, where he held the office of mayor. In 1927 he was appointed medical officer under the Children's Welfare and Public Relief Department and under the Gaols and Prisons Department, retiring in 1944. Ernest Wilson was president of the South Australian Branch of the British Medical Association in 1931-1932, was a Knight of Grace of the Venerable Order of the Hospital of Saint John of Jerusalem, a past chairman of the South Australian Branch of the Saint John Ambulance Association, a president of the Royal Society of Saint George, and on the committees of the English Speaking Union, the Home for Incurables, Minda, and the Home for Crippled Children.

His interest in historical aspects of the early days of South Australia made him a valued member of the South Australian Branch of the Royal Geographical Society of Australasia, whose meetings he seldom missed. In 1911 he married Nellie Edith, younger daughter of the late William Strawbridge, I.S.O., Surveyor-General, who, with his three daughters, Honor, Yvette and Shirley, only son, Charles, and two grandchildren, survives him. In his early days, Ernest Wilson was proficient in many branches of sport and, as might be expected from his ancestry, he took a keen interest in natural history. His genial personality will be much missed in medical and scientific circles, as well as by his many friends. His was a type of which our profession may well be proud, for not only was he a sound and thorough practitioner and a good civil servant, but also he accepted that call for service to the community that hall-marks the best amongst our members.

Dr. E. A. H. Russell writes: The late Charles Ernest Cameron Wilson was born at Bridge Street, Kensington, South Australia, on September 27, 1875. "Ernie" Wilson received his early education (1887-1889) at Pulteney Grammar School, Adelaide, from which he was granted a scholarship to enter Saint Peter's School Collegiate (1890-1893). He played tennis for Saint Peter's College against Prince Alfred College in 1892, this being the first intercollegiate tennis match to be contested between these two colleges. He was a member of the Saint Peter's College football team for three consecutive years, and played in his school eleven in 1893. Commencing medicine in 1894, he migrated to the University of Melbourne in 1897, in common with all other senior medical students in Adelaide, owing to the unfortunate disagreement between the honorary staff of the Adelaide Hospital and the Government of the day. Wilson entered Trinity College, Melbourne, and graduated in medicine in 1899. In 1900 he was house surgeon at the Melbourne General and Women's Hospitals, and later at the Adelaide Children's Hospital. In 1901 he did post-graduate study at the West London General Hospital and at Manchester. Returning to South Australia he entered into private practice in the Wallaroo-Kadina district. In 1894-1895 Wilson played lacrosse in the University of Adelaide "A" team, and in 1897 he played for the University of Melbourne when he excelled at "point". In 1899 he was captain of the University of Melbourne team. Each of the above teams was premier of its respective State. In 1898 he played for Victoria against South Australia. He was a golf enthusiast and won the Peninsula golf championship in 1920 and the public services championship in 1935. Wilson sat in the District Council of Wallaroo and Kadina for five years, was mayor for two years, and medical officer of health for fourteen years. He received a commission (captain) in 1914 and performed various home service duties during 1914-1918 in the Commonwealth Military Forces. He was a lecturer and examiner for the Saint John Ambulance Association from

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED FEBRUARY 9, 1952.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.[2]	Australia.[3]
Acute Rheumatism	..	..	..	..	..	..	..	..	..
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	..	5(2)	..	..	1	1	..	7
Diphtheria	3(1)	5(1)	..	..	3(2)	..	..	..	11
Dysentery (Bacillary)	..	8(8)	19(18)	..	1(1)	..	..	..	28
Encephalitis	..	..	..	..	..	..	1	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1(1)	..	..	..	..	..	..	1
Infective Hepatitis	..	..	..	..	13(2)	..	..	..	13
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	1	..	..	..	1
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(1)	1(1)	..	..	5	1(1)	..	..	9
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	8(5)	6(1)	6(1)	45(11)	..	..	..	..	65
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	3(2)	..	..	..	..	..	..	3
Salmonella Infection	..	..	..	..	..	..	1	..	1
Scarlet Fever	5(4)	15(9)	6(1)	5(4)	..	8(4)	..	..	39
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1(1)	1	..	..	..	..	..	2
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	37(28)	32(23)	26(19)	6(6)	17(14)	2	2	..	122
Typhoid Fever	1(1)	..	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	1(1)	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from the Australian Capital Territory.

1909 and a former chairman of the Hospitallers' Club in South Australia. Elected to the Saint John Association committee in 1933, he became chairman in 1934, and relinquished that post in 1950 to become vice-president of the association on his promotion, as priory librarian, to the executive committee of the Priory of the Venerable Order of the Hospital of Saint John of Jerusalem in Australia. During his association with the Saint John organization he was admitted to the order in the grade of Officer in 1937, promoted Commander in 1944, and was, in 1948, further promoted to the high dignity of Knight of Grace of the Venerable Order. In 1937 he returned to England to study child delinquency. He was a member of the Council of the South Australian Branch of the British Medical Association from 1927 to 1931 and was president for the year 1929-1930. Other appointments held by the late Dr. Wilson included that of vice-president of the Royal Geographical Society, the English Speaking Union, the Crippled Children's Association and the Royal Society of St. George, and surgeon to the Ship Lovers' Society. He was a councillor to the Minda Home, the Home for Incurables, and the Aerial Medical Services. His genial personality endeared him to all his friends, and he will be sadly missed by very many of us.

ERIC FRANCIS ERBY.

WE regret to announce the death of Dr. Eric Francis Erby, which occurred on February 22, 1952, at Avalon, New South Wales.

Australian Medical Board Proceedings.

QUEENSLAND.

THE following have been registered, pursuant to the provisions of *The Medical Acts*, 1939-1948, as duly qualified medical practitioners: Bannon, Paul Edward, M.B., B.S., 1951 (Univ. Sydney); Cribb, George Desmond, M.R.C.S. (England), L.R.C.P. (London), 1939, F.R.C.S. (England), 1950; Kendall, Colin Henri Gard, M.R.C.S. (England), L.R.C.P. (London), 1948, M.B., B.S., 1950 (Univ. London); Rochester, William Ronald, M.B., B.S., 1936 (Univ. Durham), D.T.M. and H. (London), 1949; Stewart, John Alexander Pollock, M.B., Ch.B., 1944 (Univ. Glasgow); Knowles, Frederick Wilfred, M.R.C.S. (England), L.R.C.P. (London), 1950.

The following additional qualifications have been registered: Dunn, Lillias Joan, Diploma in Anæsthetics, R.C.P. and S. (London), 1951; Ogden, John Kenworthy, M.R.C.O.G., 1951; Lester, Ivan Alexander, F.R.C.S. (England), 1950; Woodburn, John William, D.C.H., R.C.P. and S. (London), 1951.

Medical Appointments.

Dr. N. B. G. Abbott has been appointed quarantine officer, Hobart, Tasmania, under provisions of the *Quarantine Act*, 1908-1950.

Dr. S. R. Gerstman has been appointed a member of the Opticians Registration Board of Victoria as a nominee of the Victorian Branch of the British Medical Association.

Dr. J. K. Adey has been appointed Inspector of Inebriates' Institutions, Victoria.

Dr. W. E. Hewitt has been appointed a public vaccinator for the Borough of Ringwood, Victoria.

Dr. J. P. Maddern has been appointed resuscitation registrar at the Royal Adelaide Hospital.

Dr. J. E. McCartney has been appointed medical bacteriologist at the Institute of Medical and Veterinary Science, Adelaide.

Dr. T. A. R. Dinning has been appointed honorary assistant neurosurgeon at the Royal Adelaide Hospital.

Dr. C. M. Gurner has been appointed honorary assistant radiotherapist at the Royal Adelaide Hospital.

Dr. J. N. Parker and Dr. J. H. Slade have been appointed honorary clinical assistants in ophthalmology at the Royal Adelaide Hospital.

Dr. J. S. Covernton has been appointed honorary assistant visiting medical officer to the Northfield Wards at the Royal Adelaide Hospital.

Dr. A. Fryberg has been appointed chairman of the Nurses and Masseurs Registration Board of Queensland.

Dr. T. H. R. Mathewson and Dr. B. F. R. Stafford have been appointed members of the Nurses and Masseurs Registration Board of Queensland.

Dr. D. J. Stanger has been appointed government medical officer at Texas, Queensland.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Degotardi, Colin Boyne, M.B., B.S., 1951 (Univ. Sydney), Workshop Road, Cardiff.

Diary for the Month.

MARCH 11.—New South Wales Branch, B.M.A.: Medical Politics Committee.
MARCH 11.—New South Wales Branch, B.M.A.: Ethics Committee.
MARCH 14.—Queensland Branch, B.M.A.: Council Meeting.
MARCH 17.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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